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Nucleophilic (Radio)Fluorination of Redox-Active Esters via Radical-Polar Crossover Enabled by Photoredox Catalysis

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ABSTRACT: We report a redox-neutral method for nucleophilic fluorination of *N*-hydroxyphthalimide esters using an Ir photocatalyst under visible light irradiation. The method provides access to a broad range of aliphatic fluorides, including primary, secondary, and tertiary benzylic fluorides as well as unactivated tertiary fluorides, that are typically inaccessible by nucleophilic fluorination due to competing elimination. In addition, we show that the decarboxylative fluorination conditions are readily adapted to radiofluorination with [¹⁸F]KF. We propose that the reactions proceed by two electron transfers between the Ir catalyst and redox-active ester substrate to afford a carbocation intermediate that undergoes subsequent trapping by fluoride. Examples of trapping with O- and C-centered nucleophiles and deoxyfluorination via *N*-hydroxyphthalimidoyl oxalates are also presented, suggesting that this approach may offer a general blueprint for affecting redox-neutral S_N1 substitutions under mild conditions.

INTRODUCTION

Aliphatic organofluorine compounds are important structural motifs in pharmaceuticals, agrochemicals, and materials, conferring valuable biological and physical properties.¹ This motif is also prominently featured in positron emission tomography (PET) radiotracers.^{1a} Consequently, the identification of mild methods for late-stage introduction of fluorine has been a longstanding goal, with distinct strategies arising using nucleophilic and electrophilic fluorine sources.² For reasons of cost, functional group compatibility, and translation to radiofluorination, researchers have sought mild methods for the preparation of fluoroalkyl groups using nucleophilic fluoride.^{1,2} In most of these methods, Csp³–F bond formation follows a bimolecular nucleophilic substitution pathway (S_N2 mechanism) and is thus limited to the preparation of activated or unhindered aliphatic fluorides (Scheme 1A).³ Indeed, the typical restrictions on substrate scope for bimolecular nucleophilic substitution reactions are even more acute for fluoride due to its low nucleophilicity and high Brønsted basicity, leading to competitive elimination.^{4,5}

Stepwise nucleophilic fluorination reactions that proceed through a carbocation intermediate (S_N1 mechanism) provide a complementary strategy to bimolecular alkyl fluoride synthesis, enabling access to unactivated and hindered aliphatic fluorides. However, the generation of carbocation intermediates typically requires harsh Brønsted⁶ or Lewis acidic conditions⁷ that show poor functional group tolerance and lead to elimination and rearrangement pathways (Scheme 1B). To overcome these limitations, researchers have recently explored new strategies for carbocation generation under non-acidic conditions. The Knowles group introduced a methodology to access carbocation

Scheme 1. Nucleophilic fluorination

A. Bimolecular nucleophilic substitution (S_N2) with fluoride

- Limited to 1° & 2° aliphatic fluorides; 3° inaccessible
- Elimination competitive

B. Lewis or Brønsted acid-facilitated S_N1

- Caustic reagents preclude late-stage functionalization
- Access to 3° fluorides

C. Photocatalyzed S_N1 via mesolytic cleavage (Knowles)

- C–C, C–N, C–O bond formation

D. Electrochemical oxidation S_N1 (Baran)

- 4 examples

E. This work: Redox-neutral, radical-polar crossover S_N1 substitution

- Redox neutral
- Broad FG tolerance and mild conditions
- Access to 1°, 2°, 3° fluorides

intermediates via mesolytic cleavage following the oxidation of TEMPO-derived alkoxyamine substrates,⁸ although a wide range of nucleophiles are compatible with this approach, the method was not shown to work with fluoride and the substrates can be challenging to access (Scheme 1C). Just recently, the Baran lab reported an electrochemical approach to carbocation generation from readily available carboxylic acids (Scheme 1D).⁹ The method affords access to a broad range of hindered ethers from alcohol nucleophiles and four examples of alkylfluorides from KF. Although this report has significantly advanced the state of the art, the requirement for oxidizing conditions places limits on the substrate scope and the method was not shown to be amenable to radiofluorination. This report was closely followed by the disclosure of a photocatalytic decarboxylative ether synthesis by Ohmiya, Nagao, and coworkers.¹⁰ Yet further discovery and development of complementary methods for carbocation generation are necessary to enable broad access to hindered and unactivated aliphatic fluorides, including for late-stage fluorination and radiofluorination, as well as expanding the repertoire for additional synthetic applications.

In this context, we sought to develop a redox-neutral method for carbocation generation via radical-polar crossover^{10,11} from *N*-hydroxyphthalimide esters (Scheme 1E). We selected redox active esters as a substrate class since numerous research groups have recently reported their use as precursors to alkyl radicals via single-electron reduction and decarboxylation with release of a non-nucleophilic leaving group.¹² We hypothesized that upon single electron reduction of the substrate by the excited state of a suitable photoredox catalyst, the resulting radical could be oxidized to the corresponding carbocation by the oxidized photocatalyst and subsequently trapped with fluoride.¹³ Given the similar trends in stability between radical and carbocation species,¹⁴ we anticipated that highly substituted aliphatic substrates should be particularly amenable to both radical and carbocation generation in a radical-polar crossover, thereby expanding the scope of aliphatic fluorides available via nucleophilic fluorination. This approach would also provide a useful complement to radical methodologies for decarboxylative fluorination that require oxidizing electrophilic fluorine sources¹⁵ or the combination of a nucleophilic fluoride source with a stoichiometric oxidant, as described by the Groves lab.¹⁶

Here we report a redox-neutral decarboxylative nucleophilic fluorination that delivers primary, secondary, and tertiary benzylic fluorides and unactivated tertiary fluorides with broad functional group tolerance. We also describe mechanistic experiments that provide evidence for both radical and carbocation intermediates; in so doing, we present applications to the construction of sterically congested ethers and C–C bonds, establishing the generality of the strategy as a blueprint for affecting redox-neutral S_N1 substitutions. Finally, we show that the method is amenable to ¹⁸F-radiofluorination.

RESULTS AND DISCUSSION

Optimization. We initiated our studies with the *N*-hydroxyphthalimide ester **1** derived from naproxen, as naproxen's electron-rich arene would likely be incompatible with decarboxylative fluorination conditions that utilize electrophilic fluorine sources or stoichiometric oxidants.^{15b} Subjecting **1** to irradiation with 34 W blue LEDs in the presence of 1 mol% Ir(dF-ppy)₃ **3** and 3 equiv. of Et₃N•3HF delivered benzylic fluoride **2** in

almost quantitative yield (Table 1, Entry 1). Fluorination does not proceed in the absence of light or photocatalyst, resulting in recovery of starting material (Table 1, Entries 2 and 3). More reducing or oxidizing iridium photocatalysts were competent in the reaction, as was the organic photocatalyst 4CzIPN, all displaying high yet diminished reactivity compared to photocatalyst **3** (Table 1, Entries 4–6). While DCM was found to be the optimal solvent for the reaction, fluorination proceeded with modest to good yield in tetrahydrofuran and acetonitrile, solvents that are commonly used in radiofluorination (Table 1, Entries 7 and 8). Only trace product was observed using KF/HFIP (1,1,1,3,3,3-hexafluoroisopropanol)¹⁷ instead of Et₃N•3HF and no product was observed using KF in the absence of HFIP (Table 1, Entries 9 and 10). Although impractical from a preparative standpoint, this result provides support for possible translation to radiofluorination since [¹⁸F]KF is the most common reagent for ¹⁸F-radiochemistry (*vide infra*).¹⁸ Finally, we found that the reaction could be readily scaled to 4 mmol (Table 1, Entry 11) and photocatalyst loading could be reduced to 0.0625 mol% with minimal impact on the reaction efficiency (Table 1, Entry 12). This speaks to the practicality of the method, and the ability to use such low photocatalyst loading holds important mechanistic implications (*vide infra*).

Table 1. Optimization of Reaction Conditions.^{a,b}

entry	deviation from standard conditions	yield 2 (%) ^c
1	No deviation	99
2	No photocatalyst	0
3	No light	0
4	Ir(ppy) ₃ 4 instead of 3	96
5	[Ir(dF-CF ₃ -ppy) ₂ (dtbpy)]PF ₆ 5 instead of 3	94
6	4CzIPN 6 instead of 3	91
7	THF instead of DCM	22
8	MeCN instead of DCM	68
9	3 equiv. KF instead of Et ₃ N•3HF	0
10	3 equiv. KF/10 equiv. HFIP instead of Et ₃ N•3HF	4
11	4 mmol scale ^d	90 (75) ^e
12	0.0625 mol% Ir(dF-ppy) ₃	85

<p>3: X = F $\text{Ir}^{\text{IV}}/\text{Ir}^{\text{III}} = -1.28 \text{ V}$ $\text{Ir}^{\text{IV}}/\text{Ir}^{\text{III}} = 0.94 \text{ V}$ 4: X = H $\text{Ir}^{\text{IV}}/\text{Ir}^{\text{III}} = -1.73 \text{ V}$ $\text{Ir}^{\text{IV}}/\text{Ir}^{\text{III}} = 0.78 \text{ V}$</p>	<p>5 $\text{Ir}^{\text{IV}}/\text{Ir}^{\text{III}} = -0.89 \text{ V}$ $\text{Ir}^{\text{IV}}/\text{Ir}^{\text{III}} = 1.69 \text{ V}$</p>	<p>6 $\text{PC}^{+}/\text{PC}^{*} = -1.18 \text{ V}$ $\text{PC}^{+}/\text{PC} = 1.43 \text{ V}$</p>
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^a 0.2 mmol scale. ^b All potentials given are versus a saturated calomel electrode (SCE) and taken from ref. 19. ^c Yields determined by ¹⁹F-NMR using 1-fluoronaphthalene as an external standard. ^d General conditions except 0.4 M, 1.5 equiv. Et₃N•3HF. ^e Isolated yield.

Table 2. Substrate Scope for Photocatalytic Decarboxylative Fluorination.^a

phthalimide ester

 3 (1 mol%)

 Et₃N·3HF (3 equiv)

 34 W Blue LED

 DCM (0.2 M), rt, 4–6 h

aliphatic fluoride

 7–40

3

Primary and secondary benzylic

 7–14	7 - <i>t</i> -Bu 64% yield 8 -Ph 59% yield 9 -I 60% yield 10 -OBn 76% yield	11 -SMe 62% yield^b 12 -NHAc 73% yield 13 -OCF ₃ 60% yield^b 14 -CF ₃ 6% yield^b
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 15 63% yield	 16 40% yield^b	 17 93% yield	 18 58% yield
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 19 64% yield	 20 56% yield	 21 65% yield from ketoprofen
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α-Heteroatom

 32 28% yield^b	 33 53% yield	 34 44% yield^d
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 35 57% yield^{b,e} from trillipix	 36 56% yield from cyhalofop
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Tertiary benzylic and aliphatic

 22 87% yield	 23 3 92% yield 24 2 85% yield^{b,e} 25 1 90% yield	 26 70% yield^b	 27 40% yield^b
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 28 - <i>t</i> -Bu 76% yield^b 29 -CN 50% yield	 30 66% yield from gemfibrozil	 31 32% yield^{b,c} from enoxalone
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Multifluorinated

 37 56% yield	 38 89% yield^b from Mosher's acid	 39 52% yield
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Tertiary deoxyfluorination

 22 55% yield^{b,f}	 40 33% yield^b
--	--

from:

^a Isolated yields of an average of two runs on 0.5–1.0 mmol scale. ^b Yield determined by ¹⁹F-NMR using 1-fluoronaphthalene as an external standard. ^c 1.3:1 d.r. ^d >20:1 d.r. ^e Product unstable. ^f Yield corrected for starting material contamination with residual alcohol.

Scope Elucidation. With optimized conditions in hand, we evaluated the scope of the transformation. We found that a variety of primary benzylic fluorides could be obtained in good to excellent yields (Table 2, 7–13, 15, and 16). Several substrates bearing electron-rich functionality otherwise susceptible to oxidation under previously reported decarboxylative fluorination conditions were tolerated,^{15b} delivering dioxole 15, benzyl-protected phenol 10, and thioether 11. Fluorinated products bearing medicinally-relevant amides and trifluoromethoxy groups were generated in good yield (12 and 13). Whereas these electron-rich and electron-neutral primary benzylic phthalimide esters were competent substrates, electron-deficient substrates afforded benzylic fluorides in low yield at high conversion (14), presumably because single electron reduction and decarboxylation to the carbon-centered radical is facile but oxidation of the radical to the cation is disfavored due to the electron-withdrawing substituent.¹² As expected on the basis of this hypothesis, we found that replacing the primary benzylic substrate with a secondary substrate bearing the same substitution pattern restored reactivity, with fluorinated product 17 obtained in 93% yield.

A common limitation in nucleophilic fluorination methods that deliver secondary benzylic fluorides is elimination to styrene byproducts.^{3d,f} For all of the secondary substrates examined in Table 2, less than 5% elimination was observed, a testament to the mildness of the conditions. Indeed, even product 19 was obtained in high yield with minimal elimination despite the presence of a β-carbonyl functional group. By comparison, access to β-fluoro carbonyl derivatives by deoxyfluorination has presented a major challenge to date due to competing elimination.^{3d,f} Several handles for subsequent transition metal-mediated coupling were tolerated, including aryl iodides 9, bromides 16 and 33, and chlorides 18 and 23–26. This tolerance for easily reduced functionality can even be extended to azide-containing product 20, which was generated in 56% yield and offers a reactive handle for subsequent “click” chemistry that is widely used in bioconjugation.²¹ Additionally, basic heterocycles and heteroaromatic groups otherwise susceptible to oxidation or Minisci chemistry underwent decarboxylative fluorination in good yields (18 and 26).

In contrast to typical methods for nucleophilic fluorination, we found that access to benzylic and unactivated tertiary fluorides

is possible. For example, acyclic **22** as well as tertiary benzylic fluorides embedded within carbocyclic and heterocyclic ring systems are generated in 70–92% yield, as in the cases of **23–26**. Likewise, both cyclic and acyclic unactivated tertiary fluorides could be obtained (**27–31**). Whereas neighboring group participation may be operative in the generation of the homobenzylic tertiary fluorides **28** and **29**, it does not appear to be necessary given the success of the cyano-substituted homobenzylic fluoride **29** and fluorides **27** and **31** that do not possess a proximal nucleophilic residue. Notably, we were able to extend this protocol to the fluorination of gemfibrozil **30** in 66% yield.

Fluoroether and fluoroethioether functionality has been shown to confer unique and valuable properties to biologically active small molecules.²² We found that the redox-neutral decarboxylative nucleophilic fluorination also delivers α -oxy- and α -thioether motifs in modest to good yield (**32** and **33**). As a demonstration of the viability of the method for late-stage derivatization, fluorinated ribose **34**, trillipix-derivative **35**, and the herbicide cyhalofop-derived **36** were all readily accommodated. Likewise, application of the optimal conditions to the preparation of difluoromethyl and perfluorinated groups was successful,²³ as in the cases of **37** and **38**, and permitted the synthesis of difluorofluorene **39**, a motif featured in the hepatitis C drug ledipasvir.

Fluorine incorporation is commonly used as a bioisostere for several functionalities including C–OH and C–H bonds.^{1b} In this regard, the conversion of abundant alcohols into the corresponding alkyl fluorides via deoxyfluorination represents an attractive synthetic disconnection. However, deoxyfluorinations of tertiary alcohols to access tertiary fluorides are typically unsuccessful.²⁴ MacMillan and co-workers have recently reported a deoxyfluorination of oxalate half-esters to access tertiary fluorides.²⁵ However, the method uses an electrophilic fluorine source. Since *tert*-alkyl *N*-hydroxyphthalimidoyl oxalates are similar in redox potential to *N*-hydroxyphthalimide esters, we hypothesized that these may be amenable to the catalytic nucleophilic fluorination strategy outlined herein.²⁶ Indeed, we were pleased to find that tertiary fluorides **22** and **40** could be obtained in 55% and 33% yield from *tert*-alkyl *N*-hydroxyphthalimidoyl oxalate esters under otherwise identical conditions. Since these substrates are readily available from alcohols, the method represents a complementary approach to nucleophilic deoxyfluorination which is typically limited to primary and secondary alcohols.^{3a–f}

Mechanistic Investigations. We propose that excited **3** ($E_{1/2}^* = -1.28$ vs. SCE^{19a}) undergoes single electron transfer (SET) with the *N*-hydroxyphthalimide ester **A** (~ -1.3 V vs SCE²⁰) (Figure 2). Fragmentation of the resulting phthalimide ester radical anion and subsequent extrusion of carbon dioxide generates carbon-centered radical **B**. Radical intermediate **B** ($E_{1/2}^{ox} < 0.73$ V vs. SCE for 1° benzylic, $E_{1/2}^{ox} = 0.09$ V vs. SCE for tertiary aliphatic^{13b}) is then oxidized by photocatalyst **3**⁺ ($\text{Ir}^{\text{IV}}/\text{Ir}^{\text{III}}$ $E_{1/2} = 0.94$ V vs. SCE^{19a}), turning over the photocatalyst and furnishing carbocation **C**. Finally, this carbocation is trapped by the fluoride source to furnish the desired alkyl fluoride **D**.

A number of experimental observations provide support for the proposed mechanism. Stern–Volmer quenching analysis of the individual components of the reaction mixture indicates that the phthalimide ester quenches the excited state photocatalyst with an observed K_{SV} of $4.7 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$, which is similar to the quenching rate of the reaction mixture.²⁷

Figure 2. Mechanistic Proposal.

Figure 3. Radical and Cation Trapping.^a

^a General conditions: 1 mol% $\text{Ir}(\text{dF-ppy})_3$, 0.2 mmol **41**, 3 equiv. $\text{Et}_3\text{N}\cdot 3\text{HF}$.

^b 1.5 equiv. of TEMPO. ^c 1.5 equiv. of methyl acrylate. ^d 1.5 equiv. styrene. ^e

3 equiv. of trimethoxybenzene and 0.3 equiv. $\text{Et}_3\text{N}\cdot 3\text{HF}$. ^f 5 equiv. phenol and 0.3 equiv. $\text{Et}_3\text{N}\cdot 3\text{HF}$. ^g 6 equiv. methanol and 0.3 equiv. of $\text{Et}_3\text{N}\cdot 3\text{HF}$.

^h 5 equiv. of HFIP and run for 24 hrs; ¹⁹F-NMR yield vs external 1-fluoronaphthalene.

The quantum yield of this fluorination reaction is 0.37, indicating that chain mechanisms are unlikely or inefficient.^{27,28} This result, combined with the observation that the fluorinations proceed with high reaction efficiency at extremely low photocatalyst loadings (0.0625% of **3** in Table 1, Entry 12), suggests that the reaction is unimolecular in photocatalyst.

Subjecting tertiary phthalimide ester **41** to the fluorination conditions in the presence of several known radical traps provides evidence for the intermediacy of a radical. For example, addition of TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy) to the reaction resulted in complete inhibition of fluorination, with concomitant detection of TEMPO adduct **42** (Figure 3). In the presence of methyl acrylate, radical addition product **43** was observed, along with a diminished yield of tertiary fluoride **30** (66% isolated vs. 45% by ^{19}F -NMR in the presence of methyl acrylate). However, fluoride is not incorporated into **43**, presumably because radical oxidation adjacent to the ester carbonyl is unfavorable. On the other hand, conducting the fluorination reaction in the presence of 1.5 equiv. styrene afforded a new fluorinated product **44** in addition to the direct fluorination product **30**. **44** is most likely generated via addition of radical **B** to the styrene followed by oxidation of the resulting benzylic radical and trapping with fluoride. Evaluation of a series of electronically differentiated styrene substrates, and the outcome of the reaction with methyl acrylate, provide evidence against an alternative pathway wherein radical oxidation to cation **C** precedes olefin addition.²⁷

As a test for the intermediacy of a carbocation, we investigated whether other polar nucleophiles could be used in the decarboxylative substitution reaction. Notably, we found that C- and O-centered nucleophiles were competent with only minor changes to the reaction parameters (Table 3, **45–48**).²⁹ For example, trimethoxybenzene underwent addition to generate benzhydryl **45** in 81% yield. This reaction represents a Lewis-acid-free Friedel–Crafts substitution using abundant carboxylic acid precursors in place of alkyl halide substrates. Likewise, several alcohol nucleophiles delivered ether products **46–48** in good yield. The broad tolerance for a range of nucleophiles, including sterically hindered and poorly nucleophilic species, implicates the intermediacy of a carbocation and demonstrates the generality of the strategy to effect a range of challenging substitution reactions under remarkably mild conditions.

Radiochemistry. Aliphatic ^{18}F -radiolabelled PET tracers are almost exclusively prepared by nucleophilic substitution of alkyl sulfonates with ^{18}F]KF in the presence of a phase transfer reagent Kryptofix 2.2.2 (K_{222}).¹⁸ As such, access to high specific activity radiolabeled targets bearing unactivated secondary or tertiary fluorides remains a critical challenge. Moreover, the harsh conditions necessary for substitution of even primary or activated secondary substrates (>100 °C and high basicity) are often not suitable for late-stage radiofluorination and often lead to inseparable olefin byproducts.¹⁸ We anticipated that successful translation of the photocatalytic decarboxylative nucleophilic fluorination method would therefore enable access to previously challenging or impossible to prepare radiotracers.

To translate our method, we elected to pursue the decarboxylative radiofluorination in acetonitrile to avoid any potential clinical issues with dichloromethane. Testing the radiofluorinations in CH_3CN using ^{18}F]KF/ K_{222} as fluoride source, we found that the previously optimized photocatalyst **3** was no longer the most effective, with $\text{Ir}(\text{F-ppy})_3$ instead affording the highest radiochemical incorporation (Table 3, Entries 1 and 4–7).²⁷ No radiofluorination was observed in the absence of light or photocatalyst as determined by radio-TLC or radio-HPLC (Table 3, Entries 2 and 3). While we had previously found that HFIP was necessary for achieving fluorination using ^{19}F]KF under the “cold” conditions (Table 1, Entries 10 and 11), the addition of HFIP proved detrimental in the radiochemical system (Table 3,

Entry 9). Under the optimal conditions, the reaction is particularly fast, furnishing ^{18}F]2 in 62% radiochemical conversion (RCC) within 2 minutes of irradiation (Table 3, Entry 8). The radiofluorination was also scalable (1850–3700 MBq), permitting isolation of sufficient quantities of ^{18}F]2 to determine its molar activity ($33.7 \pm 18.9 \text{ MBq/nmol}$), which is on par with other no-carrier added nucleophilic fluorination protocols.^{17,18,30} Notably, these radiochemical reactions were conducted in a 3D-printed apparatus that permits automated handling of radioactivity with irradiation taking place from the bottom of the vials.²⁷

Table 3. Development of Radiochemical Protocol.^a

Entry	Deviation from Standard Conditions	RCC (%) ^b
1	none	64 _{n=2}
2	no photocatalyst	0 _{n=1}
3	no light	0 _{n=2}
4	3 instead of $\text{Ir}(\text{F-ppy})_3$	6 _{n=2}
5	$\text{Ir}(\text{CF}_3\text{-ppy})_3$ instead of $\text{Ir}(\text{F-ppy})_3$	43 _{n=2}
6	$\text{Ir}(\text{dF-}t\text{-Bu-ppy})_3$ instead of $\text{Ir}(\text{F-ppy})_3$	24 _{n=2}
7	$\text{Ir}(\text{F-}t\text{-Bu-ppy})_3$ instead of $\text{Ir}(\text{F-ppy})_3$	49 _{n=2}
8	2 min instead of 10 min	62 _{n=1}
9	100 μL HFIP added	33 _{n=2}

^a Typical reaction conditions: 5.3 μmol **1**, 16 mol% photocatalyst, 0.7 mL MeCN, and ^{18}F]F-/ K_2CO_3 / K_{222} (~370 MBq of activity per reaction). ^b RCC was determined by radio-TLC with number of replicates noted.

Table 4. Scope of Photocatalyzed Radiofluorination.

<p>[^{18}F]2 49 ± 7% RCC^a (n=5) 11 ± 2% RCC^b (n=3)</p>	<p>[^{18}F]30 9 ± 2% RCC^{a,c} (n=5)</p>	<p>[^{18}F]34 42 ± 15% RCC^{a,d} (n=5)</p>

^a Typical reaction conditions: 5.3 μmol **1**, 0.6 mg $\text{Ir}(\text{F-ppy})_3$, 0.7 mL MeCN, and ^{18}F]F-/ K_2CO_3 / K_{222} (~370 MBq of activity per reaction). RCC was determined by radio-TLC with number of replicates noted. ^b Reactions were conducted with 1850–3700 MBq of activity per reaction). ^c Reactions conducted using photocatalyst **3**. ^d Product identity confirmed via TLC.

Access to ^{18}F]2 is significant since its synthesis by $\text{S}_{\text{N}}2$ displacement with ^{18}F]KF would likely be plagued by rapid formation of elimination byproduct. We also briefly explored application of the radiofluorination conditions to the radiosynthesis of other fluorinated motifs that are challenging to access using conventional methods. For example, the radiofluorination protocol is amenable to the installation of a tertiary fluoride: ^{18}F]30 derived from gemfibrozil was obtained in 9 ± 2% RCC. Furthermore, we found that ribose analogue ^{18}F]34 could be

prepared in 42% RCC. In this case, the sulfonate precursor readily decomposes at room temperature, severely limiting access to radiolabeled ribose analogues by conventional substitution reactions.³¹

CONCLUSION

We have developed a photocatalytic method for nucleophilic fluorination of *N*-hydroxyphthalimide esters that exploits the redox activity of radicals as a route to carbocation formation. The approach generates a variety of useful fluorinated motifs under mild conditions and is compatible with functional groups that challenge other synthetic methods using both nucleophilic and electrophilic fluorine sources, such as access to tertiary aliphatic fluorides and tolerance to electron-rich functionality. Moreover, translation of the method to a radiochemical protocol was possible, enabling radiofluorination of derivatives of bioactive molecules. We present a preliminary demonstration of the generality of this approach to redox-neutral S_N1-like substitutions in extensions to a new substrate class, such as deoxyfluorination of tertiary *N*-hydroxyphthalimidoyl oxalates, and to new nucleophiles, as in the construction of sterically congested ethers and C–C bonds.

ASSOCIATED CONTENT

Supporting Information

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

Experimental procedures and characterization and spectral data for new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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Supporting Information

Nucleophilic (Radio)Fluorination of Redox-Active Esters via Radical-Polar Crossover Enabled by Photoredox Catalysis

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I. General Information

General Procedures. Unless otherwise noted, reactions were performed with exclusion of air and moisture. Solvent was freshly distilled/degassed prior to use unless otherwise noted. Organic solutions were concentrated under reduced pressure using a rotary evaporator (25 °C, < 50 torr). Automated column chromatography was performed using silica gel cartridges on a Biotage SP4 (40–53 μm , 60 Å). SiliaFlash® Irregular silica gel P60 (40–63 μm , 230–400 mesh) was used as received. Preparatory thin layer chromatography was conducted on SiliaPlate TLC Glass Backed TLC Extra Hard Layer, 60 Å, 20 cm x 20 cm, 1000 μm thickness.

Materials. Commercial reagents were purchased from Sigma Aldrich, VWR, Fisher, Oakwood, or Strem, and used as received. Dichloromethane (DCM), tetrahydrofuran (THF), acetonitrile (MeCN), dimethylformamide (DMF), dimethyl sulfoxide (DMSO), toluene and dioxane were dried by passing through activated alumina columns and sparged with nitrogen before use. Photocatalysts used were purchased from Stem or Sigma Aldrich and were used as received and stored on the benchtop. Phthalimide esters were prepared according to general procedures and stored on the benchtop. Triethylamine trihydrofluoride was obtained from Sigma Aldrich and was stored on the benchtop.

Instrumentation. Proton nuclear magnetic resonance (^1H -NMR) spectra were recorded on a Bruker 500 AVANCE spectrometer (500 MHz), a Bruker NanoBay 300 spectrometer (300 MHz), or Varian Unity Inova (400 MHz). Proton chemical shifts are reported in parts per million downfield from tetramethylsilane and referenced to residual protium in the NMR solvent ($\text{CDCl}_3 = \delta$ 7.26 ppm, $\text{CD}_3\text{CN} = \delta$ 1.94 ppm, $\text{CD}_2\text{Cl}_2 = \delta$ 5.32 ppm). Carbon nuclear magnetic resonance (^{13}C -NMR) spectra were recorded on a Bruker 500 AVANCE spectrometer (126 MHz) or a Varian Inova spectrometer (100 MHz). Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent residual peak ($\text{CDCl}_3 = \delta$ 77.16 ppm, $\text{CD}_2\text{Cl}_2 = \delta$ 53.84 ppm, $\text{CD}_3\text{CN} = \delta$ 1.32 ppm). ^1H -decoupled ^{19}F -NMR spectra (282 MHz) were recorded on a Bruker NB 300 spectrometer (used for yield determination versus external standard); ^1H -coupled ^{19}F -NMR spectra were recorded on a Bruker 500 AVANCE spectrometer (470 MHz), a Bruker NanoBay 300 spectrometer (282 MHz), or Varian Unity Inova (376 MHz); chemical shifts are reported in parts per million. NMR data are represented as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet; higher order splitting is specifically noted), coupling constant in Hertz (Hz), integration. High-resolution mass spectra were obtained on an Agilent 6220 using electrospray ionization time-of-flight (ESI-TOF) or on an Agilent 7200 GC-QTOF. FT-IR spectra were recorded on a Perkin-Elmer Spectrum 100 or on a Thermo Nicolet 6700 and are reported in terms of frequency of absorption (cm^{-1}). UV-Vis spectra were recorded on an Agilent Cary 60 UV-VIS Spectrometer. Fluorescence measurements were obtained on an Agilent Cary Eclipse fluorescence spectrophotometer.

Lamps utilized were 34 watt Kessil H150 Blue. For the emission spectrum of Kessil H150 Blue, see Shields, *et. al.*¹ For quantum yield determination, a Kessil PR160-440 nm lamp was utilized and set to 50% power as the emission spectrum was more monochromatic compared to the Kessil H150 Blue.

II. General Procedures

General Procedure A: Phthalimide Ester Synthesis with DIC

This general procedure was adapted from Weix, *et. al.*² An oven-dried flask with a stir bar was charged with carboxylic acid (4.00 mmol, 1 equiv.), followed by *N*-hydroxyphthalimide (978 mg, 6.00 mmol, 1.5 equiv.), and 4-dimethylaminopyridine (DMAP, 24.4 0.2 mmol, 0.05 equiv.). The flask was septa capped and placed under N_2 . The flask was charged with THF (20 mL) followed by *N,N'*-diisopropylcarbodiimide (DIC, 0.87 mL, 5.6 mmol, 1.4 equiv.) and stirred overnight. Then, the reaction mixture was filtered through a glass frit. The filtered solids were rinsed three times with EtOAc or DCM (40 mL). The combined filtrates were concentrated via rotary evaporation to yield an orange or yellow solid residue. The residue was subjected to column chromatography. The resulting phthalimide ester was dried overnight under vacuum and subsequently characterized.

General Procedure B: Phthalimide Ester Synthesis via Acid Chloride

This general procedure was adapted from Fu, *et. al.*³ An oven-dried flask with a stir bar was charged with carboxylic acid (4.00 mmol, 1 equiv.). The flask was septa capped and placed under N_2 . The flask was charged with 20 mL of DCM and 5 drops of DMF (~10 μL , catalytic). Oxalyl chloride (0.60 mL, 7.1 mmol, 1.75 equiv.) was added dropwise with a vent needle in place to allow for gas evolution. The reaction mixture typically went from heterogenous to homogenous, if the carboxylic acid was insoluble, as the reaction proceeded. After gas evolution had stopped (30 min

to 2 hr), the reaction mixture was concentrated via rotary evaporation to remove any remaining oxalyl chloride. Following concentration, the flask containing the crude acid chloride was charged with *N*-hydroxyphthalimide (685 mg, 4.20 mmol, 1.05 equiv.). The flask was placed under N₂ and charged with 20 mL of anhydrous DCM. The mixture was stirred and triethylamine (0.580 mL, 4.20 mmol, 1.05 equiv.) was added dropwise via syringe and additional gas evolution was observed. The reaction was usually slightly red/orange, indicative of deprotonated *N*-hydroxyphthalimide. The reaction mixture was stirred overnight at room temperature. The reaction mixture was then concentrated via rotary evaporation. The resulting residue was taken up in DCM and subjected to column chromatography. The resulting phthalimide ester was dried overnight under vacuum and subsequently characterized.

General Procedure C: Phthalimide Ester Synthesis with EDC

An oven-dried 50 mL flask, equipped with a stir bar, was charged with the appropriate carboxylic acid (4.00 mmol, 1.00 equiv.), *N*-hydroxyphthalimide (717 mg, 4.40 mmol, 1.10 equiv.), DMAP (24.4 mg, 0.200 mmol, 0.0500 equiv.), and *N*-(3-Dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (EDC•HCl, 805 mg, 4.20 mmol, 1.05 equiv.). The flask was placed under nitrogen and charged with 20 mL of THF. The reaction mixture was stirred for 6-12 hours. Upon completion, the reaction mixture was poured into water and the aqueous layer was extracted 3 times with DCM (60 mL). The organics were washed with sat. NaHCO₃ and then water. The organics were dried over sodium sulfate, filtered, and then concentrated via rotary evaporation. The resulting residue was subjected to column chromatography. The resulting phthalimide ester was dried overnight under vacuum and subsequently characterized.

General Procedure D: Screening Scale (0.2 mmol scale)

An oven-dried 1-dram vial with a stir bar was charged with 1.5 mg of Ir(dF-ppy)₃ (1.5 mg, 0.0020 mmol, 0.010 equiv.) and appropriate phthalimide ester (0.200 mmol, 1 equiv.). The vial was then charged with triethylamine•3HF (97.8 uL, 0.600 mmol, 3.00 equiv.). The vial was septa capped and wrapped with labeled electrical tape. The vial was frozen in a -78 °C bath and subjected to 3 cycles of evacuation/backfill with nitrogen via spaghetti line. Following this, the vial was placed under N₂ and charged with degassed DCM (1.00 mL) via syringe. The spaghetti line was removed, and the vial was placed 3 cm in front of a 34 W H150 Blue Kessil Lamp with 2 fans for cooling. Usually gas evolution was observable. The vials were irradiated for 4-6 hours approximately. Upon completion, the vials were charged with 26.0 uL of 1-fluoronaphthalene (0.201 mmol, 1.00 equiv.) and subjected to analysis by ¹H-decoupled, ¹⁹F-NMR.

General Procedure E: Isolation scale (0.6 mmol scale)

An oven-dried 2-dram vial with a stir bar was charged with of Ir(dF-ppy)₃ (4.6 mg, 0.006 mmol, 0.01 equiv.) and appropriate phthalimide ester (0.600 mmol, 1 equiv.). The vial was then charged with triethylamine•3HF (3 x 97.8 uL, 1.8 mmol, 3.00 equiv.). The vial was placed in a -78 °C bath and subjected to 3 cycles of evacuation/backfill via spaghetti line. Following this, the vial was placed under N₂ and charged with degassed DCM (3.00 mL) via syringe. The spaghetti line was removed, and the vial was placed 3 cm in front of a 34 W H150 Blue Kessil Lamp with 2 fans for cooling. Usually gas evolution was observable. The vials were irradiated for 4-6 hours. Upon completion, the vials were loaded onto silica gel for column chromatography or filtered through a silica/cotton plug and concentrated before being subjected to preparatory TLC.

Figure S1: Set-up for Screening and Isolation Scale Fluorination Reactions.

Left: Isolation (left) and screening scale (right) in photocatalysis set up. Right: Screening-multiple vials per lamp, isolation-one vial per lamp.

III. Selected Optimization Studies

Table S1. Photocatalyst Evaluation.

0.2 mmol scale, Determined via ¹⁹F-NMR vs. external 1-fluoronaphthalene

Note: With poorer performing substrates, the photocatalysts delivered a wider range in effectiveness; in those cases, Ir(dF-ppy)₃ performed best.

Table S2. Phthalimide Ester Evaluation.

Entry	Deviation in conditions	¹⁹ F-NMR Yield (%)
1	1	99
2	S1	78

Table S3. Photocatalyst Loading.

Entry	Deviation in conditions	¹⁹ F-NMR Yield (%)	TON
1	None-1 mol% Ir(dF-ppy) ₃	94	94
2	0.5 mol% Ir(dF-ppy) ₃	91	182
3	0.25 mol% Ir(dF-ppy) ₃	89	356
4	0.125 mol% Ir(dF-ppy) ₃	84	672
5	0.0625 mol% Ir(dF-ppy) ₃	85	1360
6	0.01 mol% Ir(dF-ppy) ₃ ^b	46	4600

^aYields determined by ¹⁹F-NMR vs external 1-fluoronaphthalene^bIncomplete conversion observed at 4 hours

Table S4. Solvent Evaluation.

Entry	Deviation in conditions	¹⁹ F-NMR Yield (%) ^a
1	DCM	98
2	Dioxane	24
3	DMF	7
4	DMSO	2
5	MeCN	68
6	THF	22

^aYields determined by ¹⁹F-NMR vs external 1-fluoronaphthalene

Table S5. Fluoride Loading.

Entry	Deviation in conditions	¹⁹ F-NMR Yield (%) ^a
1	None (3 eq. Et ₃ N·3HF)	101
2	2 eq. Et ₃ N·3HF	99
3	1 eq. Et ₃ N·3HF	87
4	0.75 eq. Et ₃ N·3HF	81
5	0.5 eq. Et ₃ N·3HF	67
6	0.25 eq. Et ₃ N·3HF	56*

*relative to fluoride, 42% relative to phthalimide ester

^aYields determined by ¹⁹F-NMR vs external 1-fluoronaphthalene

Table S6. Fluoride Source Screening.

Entry	Deviation in conditions	¹⁹ F-NMR Yield (%) ^a
1	Et ₃ N·3HF	93
2	KF	0
3	KF + HFIP (10 equiv)	4
4	KF + 18-crown-6 (1 equiv)	Trace

^aYields determined by ¹⁹F-NMR vs external 1-fluoronaphthalene

IV. Synthesis and Characterization of Phthalimide Esters and Oxalates

1,3-dioxoisindolin-2-yl 2-(6-methoxynaphthalen-2-yl)propanoate (1)

According to general procedure A, to an oven dried 50-mL flask with a stir bar was added 2-(6-Methoxy-2-naphthyl)propionic acid (926.8 mg, 4.00 mmol, 1.00 equiv.), *N*-hydroxyphthalimide (992.6 mg, 6.08 mmol, 1.5 equiv.), and DMAP (23.8 mg, 0.195 mmol, 0.05 equiv.). The flask was septa capped and placed under N₂. The flask was then charged with 20 mL of anhydrous THF followed by DIC (0.87 mL, 5.58 mmol, 1.4 equiv.). The flask was stirred overnight. The reaction started an orange color that faded to a pale yellow color as the reaction proceeded. Upon completion, the reaction mixture was filtered through a frit. The filtered solids were washed with EtOAc 3 times. The combined filtrate was concentrated via rotary evaporation to yield a yellow residue. The residue was taken up in EtOAc and subjected to column chromatography (10 to 30% EtOAc in hexanes). This afforded 1,3-dioxoisindolin-2-yl 2-(6-methoxynaphthalen-2-yl)propanoate as a white solid (1.3093 g, 3.488 mmol, 87%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.86 (dd, *J* = 5.6, 3.1 Hz, 2H), 7.82 – 7.73 (m, 5H), 7.49 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.23 – 7.08 (m, 2H), 4.26 (q, *J* = 7.1 Hz, 1H), 3.92 (s, 3H), 1.75 (d, *J* = 7.2 Hz, 3H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 171.07, 158.03, 134.87, 134.14, 133.59, 129.59, 129.09, 127.69, 126.52, 126.04, 124.08, 119.35, 105.79, 55.48, 43.09, 19.17. (2 carbon peaks are obscured by overlap)

HRMS: (ESI-TOF) calculated for C₂₂H₁₈NO₅⁺ ([M+H]⁺): 376.11795, found 376.11723.

FTIR (thin film, cm⁻¹): ν 2942 (w), 1809 (m), 1783 (m), 1738 (s), 1632 (m), 1607 (m), 1504 (w), 1488 (m), 1463 (m), 1419 (w), 1368 (m), 1276 (m), 1260 (m), 1239 (m), 1216 (m), 1184 (m), 1164 (m), 1138 (s), 1080 (m), 1039 (s), 1013 (s), 1001 (s), 964 (m), 926 (m), 896 (m), 878 (m), 850 (s), 821 (m), 783 (m), 757 (m), 693 (s), 660 (m).

4,5,6,7-tetrachloro-1,3-dioxoisindolin-2-yl 2-(6-methoxynaphthalen-2-yl)propanoate (S1)

Synthesized according to general procedure A with 2-(6-Methoxy-2-naphthyl)propionic acid (936.8 mg, 4.09 mmol, 1 equiv), *N*-hydroxytetrachlorophthalimide (1,743.6 mg, 5.79 mmol, 1.5 equiv), DMAP (28.5 mg, 0.2 mmol, 0.05 equiv) and DIC (0.87 mL, 5.58 mmol, 1.4 equiv). Purified over silica with flash chromatography (10 to 50% DCM in hexanes) and fractions containing product were isolated in a flask and subjected to recrystallization with hot DCM. MeOH was added and the flask was cooled for several hours. A fluorescent yellow solid was observed to precipitate and the solid was isolated on a frit. The solid was transferred to a vial and dried overnight *in vacuo* to afford the title compound as a flocculant, fluorescent yellow solid (1.3314 g, 2.595 mmol, 64%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.84 – 7.70 (m, 3H), 7.46 (dd, *J* = 8.4, 1.9 Hz, 1H), 7.16 (dd, *J* = 8.8, 2.5 Hz, 1H), 7.13 (d, *J* = 2.5 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 1H), 3.92 (s, 3H), 1.74 (d, *J* = 7.2 Hz, 3H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 170.47, 157.97, 141.00, 134.06, 132.98, 130.43, 129.45, 128.92, 127.69, 126.40, 125.75, 124.69, 119.30, 105.64, 55.36, 42.87, 18.86. (1 carbon peak is obscured by overlap)

HRMS: (ESI-TOF) calculated for C₂₂H₁₄³⁵Cl₄NO₅⁺ ([M+H]⁺): 511.96206, found 511.96121.

Calculated for C₂₂H₁₄³⁵Cl₃³⁷ClNO₅⁺ ([M+H]⁺): 513.95937, found 513.95783.

Calculated for C₂₂H₁₄³⁵Cl₂³⁷Cl₂NO₅⁺ ([M+H]⁺): 515.95684, found 515.95721.

FTIR (thin film, cm⁻¹): ν 2939 (w), 1821 (w), 1795 (m), 1743 (s), 1631 (w), 1604 (m), 1502 (w), 1485 (w), 1461 (w), 1392 (w), 1378 (s), 1362 (m), 1350 (m), 1301 (m), 1262 (m), 1217 (m), 1197 (m), 1155 (s), 1124 (w), 1101 (w), 1078 (m), 1046 (s), 1031 (s), 997 (s), 958 (w), 926 (w), 883 (m), 856 (s), 847 (s), 810 (s), 791 (m), 774 (w), 746 (m), 729 (s), 712 (s), 684 (m), 661 (w), 650 (w), 619 (m), 588 (w), 579 (w), 555 (w), 474 (s), 440 (m), 405 (w).

1,3-dioxoisindolin-2-yl 2-(4-(*tert*-butyl)phenyl)acetate (S2)

Synthesized according to general procedure A with 2-(4-(*tert*-butyl)phenyl)acetic acid (754.8 mg, 3.93 mmol, 1 equiv.), *N*-hydroxyphthalimide (964.4 mg, 6.00 mmol, 1.5 equiv.), DMAP (23.0 mg, 0.21 mmol, 0.05 equiv.) and DIC (0.87 mL, 5.58 mmol, 1.4 equiv.). Purified over silica with flash chromatography (10 to 20% EtOAc in hexanes) to afford the title compound as a white solid (1.2663 g, 3.753 mmol, 96%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.89 (dd, J = 5.5, 3.1 Hz, 2H), 7.79 (dd, J = 5.5, 3.1 Hz, 2H), 7.40 (d, J = 8.3 Hz, 2H), 7.32 (d, J = 8.4 Hz, 2H), 3.97 (s, 2H), 1.32 (s, 9H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 167.99, 162.03, 150.84, 134.93, 129.07, 129.05, 128.59, 125.98, 124.14, 37.31, 34.69, 31.45.

HRMS: (ESI-TOF) calculated for C₂₀H₁₉NNaO₄⁺ ([M+Na]⁺): 360.12063, found 360.12069.

FTIR (thin film, cm⁻¹): ν 2959 (m), 1817 (m), 1788 (m), 1742 (s), 1617 (w), 1608 (w), 1466 (m), 1414 (m), 1360 (m), 1331 (m), 1311 (w), 1291 (w), 1266 (m), 1214 (m), 1184 (s), 1170 (m), 1142 (m), 1121 (m), 1061 (s), 1024 (m), 1013 (m), 972 (s), 957 (m), 935 (m), 923 (m), 877 (s), 843 (m), 824 (s), 815 (s), 789 (s), 784 (s), 770 (w), 724 (m), 713 (m), 696 (s), 619 (w), 579 (m), 553 (s), 518 (s), 494 (m), 486 (m), 424 (w), 403 (w).

1,3-dioxoisindolin-2-yl 2-([1,1'-biphenyl]-4-yl)acetate (S3)

Synthesized according to general procedure A with 4-biphenylacetic acid (845.9 mg, 3.99 mmol, 1 equiv.), *N*-hydroxyphthalimide (978.3 mg, 6.00 mmol, 1.5 equiv.), DMAP (30.4 mg, 0.25 mmol, 0.05 equiv.) and DIC (0.87 mL, 5.58 mmol, 1.4 equiv.). Purified over silica with flash chromatography (10 to 30% EtOAc in hexanes) to afford the title compound as a white solid (1.3390 g, 3.747 mmol, 94%).

¹H NMR (400 MHz, Chloroform-*d*): δ 7.89 (dd, J = 5.5, 3.1 Hz, 2H), 7.79 (dd, J = 5.5, 3.1 Hz, 2H), 7.66 – 7.57 (m, 4H), 7.53 – 7.41 (m, 4H), 7.35 (t, J = 7.4, 1.3 Hz, 1H), 4.05 (s, 2H).

¹³C NMR (101 MHz, Chloroform-*d*): δ 167.82, 161.99, 140.92, 140.73, 134.95, 130.64, 129.86, 129.07, 128.93, 127.76, 127.56, 127.27, 124.16, 37.51.

HRMS: (ESI-TOF) calculated for C₂₂H₁₆NO₄⁺ ([M+H]⁺): 358.10738, found 358.10682.

FTIR (thin film, cm⁻¹): ν 3033 (w), 1817 (m), 1807 (m), 1786 (m), 1738 (s), 1611 (m), 1567 (m), 1524 (w), 1488 (m), 1469 (m), 1412 (m), 1360 (m), 1292 (m), 1213 (m), 1189 (m), 1158 (m), 1128 (m), 1101 (m), 1081 (m), 1063 (s), 1018 (m), 1007 (m), 970 (m), 897 (m), 876 (m), 839 (m), 814 (m), 793 (m), 770 (m), 748 (s), 731 (m), 690 (s).

1,3-dioxoisindolin-2-yl 2-(4-iodophenyl)acetate (S4)

Synthesized according to general procedure A with 4-iodophenylacetic acid (1.313 g, 5.00 mmol, 1 equiv.), *N*-hydroxyphthalimide (1.227 g, 7.5 mmol, 1.5 equiv.), DMAP (34.3 mg, 0.28 mmol, 0.05 equiv.) and DIC (1.1 mL, 7.06 mmol, 1.4 equiv.). Purified over silica with flash chromatography (10 to 30% EtOAc in hexanes) to afford the title compound as a white solid (1.7556 g, 4.312 mmol, 86%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.96 – 7.86 (m, 2H), 7.80 (dd, J = 5.2, 2.8 Hz, 2H), 7.71 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.3 Hz, 2H), 3.94 (s, 2H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 167.34, 161.90, 138.14, 135.01, 131.37, 131.27, 128.99, 124.19, 93.69, 37.40.

HRMS: (ESI-TOF) calculated for C₁₆H₁₀INO₄⁺ ([M+H]⁺): 407.97273, found 407.97266.

FTIR (thin film, cm⁻¹): ν 2938 (w), 1848 (w), 1814 (w), 1785 (m), 1744 (s), 1485 (m), 1463 (m), 1407 (m), 1354 (m), 1337 (m), 1186 (m), 1131 (m), 1108 (m), 1070 (s), 1059 (s), 1007 (m), 969 (m), 919 (m), 895 (m), 877 (s), 825 (m), 808 (m), 786 (s), 742 (m), 714 (m), 694 (s).

1,3-dioxoisindolin-2-yl 2-(4-(benzyloxy)phenyl)acetate (S5)

Synthesized according to general procedure A with 2-(4-(benzyloxy)phenyl)acetic acid (0.88 g, 3.63 mmol, 1 equiv.), *N*-hydroxyphthalimide (0.926 g, 5.67 mmol, 1.5 equiv.), DMAP (23.1 mg, 0.2 mmol, 0.05 equiv.) and DIC (0.7 mL, 4.5 mmol, 1.4 equiv.). Purified over silica with flash chromatography (10 to 30% EtOAc in hexanes) to afford the title compound as a white solid (1.1466 g, 2.96 mmol, 82%).

¹H NMR (500 MHz, Methylene Chloride-*d*₂): δ 7.88 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.81 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.44 (d, *J* = 7.3 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 2H), 7.36 – 7.27 (m, 3H), 6.99 (d, *J* = 8.7 Hz, 2H), 5.07 (s, 2H), 3.94 (s, 2H).

¹³C NMR (126 MHz, Methylene Chloride-*d*₂): δ 168.66, 162.37, 158.97, 137.56, 135.43, 130.98, 129.36, 129.06, 128.50, 128.10, 124.56, 124.41, 115.60, 70.52, 37.36.

HRMS: (ESI-TOF) calculated for C₂₃H₁₇NO₅⁺ ([M+H]⁺): 387.11067, found 387.11076.

FTIR (thin film, cm⁻¹): ν 3033 (w), 2934 (w), 1812 (w), 1785 (s), 1739 (s), 1612 (w), 1581 (w), 1514 (s), 1465 (m), 1450 (w), 1424 (w), 1390 (w), 1362 (w), 1346 (w), 1314 (w), 1272 (w), 1257 (w), 1234 (s), 1181 (m), 1160 (w), 1104 (s), 1078 (m), 1039 (m), 1026 (m), 1011 (w), 975 (m), 953 (m), 928 (w), 909 (w), 875 (s), 860 (w), 829 (m), 808 (m), 784 (s), 765 (m), 733 (s), 693 (s), 598 (w), 581 (w), 519 (s), 503 (m), 488 (w), 476 (w), 455 (w), 408 (w).

1,3-dioxoisindolin-2-yl 2-(4-(methylthio)phenyl)acetate (S6)

Synthesized according to general procedure A with 2-(4-(methylthio)phenyl)acetic acid (0.546 g, 3.00 mmol, 1 equiv.), *N*-hydroxyphthalimide (0.749 g, 4.59 mmol, 1.5 equiv.), DMAP (20.6 mg, 0.2 mmol, 0.05 equiv.) and DIC (0.7 mL, 4.5 mmol, 1.4 equiv.). Purified over silica with flash chromatography (10 to 30% EtOAc in hexanes) to afford the title compound as a yellow solid (0.941 g, 2.88 mmol, 96%).

¹H NMR (500 MHz, Methylene Chloride-*d*₂): δ 7.88 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.81 (dd, *J* = 5.6, 3.1 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.4 Hz, 2H), 3.96 (s, 2H), 2.49 (s, 3H).

¹³C NMR (126 MHz, Methylene Chloride-*d*₂): δ 168.38, 162.34, 139.03, 135.45, 130.27, 129.34, 128.84, 127.09, 124.43, 37.65, 15.94.

HRMS: (ESI-TOF) calculated for C₁₇H₁₃NO₄S⁺ ([M+H]⁺): 327.05653, found 327.05595.

FTIR (thin film, cm⁻¹): ν 2916 (w), 1805 (w), 1781 (m), 1738 (s), 1606 (w), 1515 (w), 1493 (m), 1465 (m), 1435 (w), 1410 (w), 1372 (m), 1349 (m), 1327 (m), 1274 (w), 1244 (w), 1212 (m), 1183 (m), 1124 (m), 1103 (s), 1077 (s), 1012 (m), 971 (s), 924 (m), 876 (s), 861 (m), 800 (m), 787 (m), 754 (s), 712 (m), 693 (s), 596 (m), 566 (m), 518 (m), 503 (s), 478 (m).

1,3-dioxoisindolin-2-yl 2-(4-acetamidophenyl)acetate (S7)

Synthesized according to general procedure C with 2-(4-acetamidophenyl)acetic acid (771.8 mg, 3.99 mmol, 1 equiv.), *N*-hydroxyphthalimide (725.1 mg, 4.45 mmol, 1.12 equiv.), DMAP (25.5 mg, 0.21 mmol, 0.05 equiv.) and EDC•HCl (812.9 mg, 4.24 mmol, 1.06 equiv.). Purified over silica with flash chromatography (30% acetone in hexanes) to afford the title compound as a cream colored solid (1.1943 g, 3.530 mmol, 88%).

Note: use of oxalyl chloride conditions (general procedure B) resulted in generation of the imidoyl phthalimide ester from the amide and use of DIC conditions (general procedure A) resulted in a difficult separation from *N,N'*-diisopropyl urea.

¹H NMR (500 MHz, Chloroform-*d*): δ 7.88 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.79 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.51 (d, *J* = 8.2 Hz, 2H), 7.33 (d, *J* = 8.2 Hz, 2H), 7.22 (broad s, 1H), 3.95 (s, 2H), 2.17 (s, 3H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 168.39, 167.81, 161.97, 137.65, 134.96, 130.10, 129.01, 127.38, 124.16, 120.24, 37.26, 24.79.

HRMS: (ESI-TOF) calculated for C₁₈H₁₅N₂O₅⁺ ([M+H]⁺): 339.09755, found 339.09730.

FTIR (thin film, cm⁻¹): ν 3120 (w), 3045 (w), 2923 (w), 2852 (w), 1809 (w), 1783 (m), 1736 (s), 1692 (m), 1642 (m), 1600 (m), 1537 (m), 1514 (m), 1467 (m), 1415 (m), 1373 (m), 1358 (m), 1326 (m), 1286 (m), 1263 (m), 1220 (m), 1184 (m), 1127 (m), 1082 (s), 1023 (m), 1015 (m), 975 (s), 951 (m), 934 (m), 877 (s), 815 (m), 789 (s), 767 (m), 715 (m), 696 (s), 640 (m), 609 (m), 584 (m), 517 (s), 506 (s), 488 (m), 411 (w), 404 (m).

1,3-dioxoisindolin-2-yl 2-(4-(trifluoromethoxy)phenyl)acetate (S8)

Synthesized according to general procedure A with 4-(trifluoromethoxy)phenylacetic acid (2.139 g, 9.72 mmol, 1 equiv.), *N*-hydroxyphthalimide (2.510 g, 15.4 mmol, 1.5 equiv.), DMAP (67.8 mg, 0.55 mmol, 0.05 equiv.) and DIC (2.3 mL, 14.8 mmol, 1.4 equiv.). Purified over silica with flash chromatography (10 to 30% EtOAc in hexanes) to afford the title compound as a yellow solid (3.4854 g, 9.542 mmol, 95%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.89 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.80 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.42 (d, *J* = 8.7 Hz, 2H), 7.23 (d, *J* = 8.1 Hz, 2H), 4.01 (s, 2H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 167.48, 161.92, 148.96, 135.04, 130.94, 130.29, 128.94, 124.21, 121.48, 120.54 (q, *J* = 257.4 Hz), 37.09.

¹⁹F NMR (282 MHz, Chloroform-*d*): δ -57.85 (s, 3F).

HRMS: (ESI-TOF) calculated for C₁₇H₁₀F₃NO₅⁺ ([M+Na]⁺): 365.05111, found 365.05174.

FTIR (thin film, cm⁻¹): ν 2973 (w), 2931 (w), 1814 (m), 1787 (m), 1745 (s), 1611 (w), 1596 (w), 1510 (m), 1469 (w), 1420 (w), 1371 (w), 1357 (w), 1314 (w), 1220 (s), 1166 (s), 1150 (s), 1101 (s), 1081 (s), 1015 (m), 977 (m), 956 (m), 926 (m), 877 (m), 794 (m), 777 (m), 764 (m), 691 (s), 654 (m), 591 (m), 517 (m), 481 (m).

1,3-dioxoisindolin-2-yl 2-(4-(trifluoromethyl)phenyl)acetate (S9)

Synthesized according to general procedure A with 4-(trifluoromethyl)phenylacetic acid (2.008 g, 9.84 mmol, 1 equiv.), *N*-hydroxyphthalimide (2.400 g, 14.7 mmol, 1.5 equiv.), DMAP (62.5 mg, 0.51 mmol, 0.05 equiv.) and DIC (2.3 mL, 14.8 mmol, 1.4 equiv.). Purified over silica with flash chromatography (10 to 30% EtOAc in hexanes) to afford the title compound as a yellow-white solid (3.253 g, 9.314 mmol, 93%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.89 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.80 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.52 (d, *J* = 7.9 Hz, 2H), 4.06 (s, 2H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 167.18, 161.88, 135.59 (q, *J* = 1.5 Hz), 135.05, 130.35 (q, *J* = 32.7 Hz), 129.88, 128.95, 125.99 (q, *J* = 3.8 Hz), 124.11 (q, *J* = 272.1 Hz), 37.60.

¹⁹F NMR (282 MHz, Chloroform-*d*): δ -62.67 (s, 3F)

HRMS: (ESI-TOF) calculated for C₁₇H₁₀F₃NO₄⁺ ([M+H]⁺): 349.05619, found 349.05637

FTIR (thin film, cm⁻¹): ν 2972 (w), 2935 (w), 1814 (w), 1786 (w), 1743 (s), 1616 (w), 1468 (w), 1420 (w), 1372 (w), 1360 (w), 1323 (m), 1244 (w), 1198 (w), 1185 (w), 1173 (m), 1158 (m), 1134 (m), 1104 (s), 1064 (s), 1015 (m), 978 (m), 960 (m), 940 (m), 877 (m), 841 (w), 805 (m), 775 (m), 753 (w), 718 (w), 692 (s), 669 (m), 634 (w), 595 (m), 518 (m), 497 (m), 482 (w), 413 (w), 405 (w).

1,3-dioxoisindolin-2-yl 2-(benzo[d][1,3]dioxol-5-yl)acetate (S10)

Synthesized according to general procedure A with 3,4-(methylenedioxy)phenylacetic acid (723.8 mg, 4.02 mmol, 1 equiv.), *N*-hydroxyphthalimide (967.1 mg, 6.00 mmol, 1.5 equiv.), DMAP (25.1 mg, 0.21 mmol, 0.05 equiv.) and DIC

(0.87 mL, 5.58 mmol, 1.4 equiv.). Purified over silica with flash chromatography (10 to 30% EtOAc in hexanes) to afford the title compound as a cream-colored solid (1.2579 g, 3.867 mmol, 96%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.91 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.81 (dd, *J* = 5.5, 3.1 Hz, 2H), 6.90 (d, *J* = 1.7 Hz, 1H), 6.87 – 6.80 (m, 2H), 5.99 (s, 2H), 3.93 (s, 2H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 167.87, 161.96, 148.16, 147.43, 134.94, 129.03, 125.05, 124.14, 122.83, 109.86, 108.67, 101.36, 37.51.

HRMS: (ESI-TOF) calculated for C₁₇H₁₂NO₆⁺ ([M+H]⁺): 326.06591, found 326.06529.

FTIR (thin film, cm⁻¹): ν 2916 (w), 1816 (m), 1788 (m), 1742 (s), 1610 (w), 1506 (m), 1495 (m), 1468 (m), 1449 (m), 1406 (w), 1358 (m), 1335 (m), 1290 (w), 1278 (w), 1246 (s), 1187 (m), 1159 (m), 1138 (m), 1065 (s), 1034 (s), 1015 (m), 970 (m), 946 (m), 925 (m), 891 (m), 878 (s), 854 (m), 819 (m), 810 (m), 792 (m), 780 (m), 743 (m), 720 (m), 695 (s).

1,3-dioxoisindolin-2-yl 2-(4-bromothiophen-2-yl)acetate (S11)

Synthesized according to general procedure A with 4-bromothiopheneacetic acid (884.7 mg, 4.00 mmol, 1 equiv.), *N*-hydroxyphthalimide (912.5 mg, 5.59 mmol, 1.5 equiv.), DMAP (20.6 mg, 0.17 mmol, 0.05 equiv.) and DIC (0.87 mL, 5.58 mmol, 1.4 equiv.). Purified over silica with flash chromatography (10 to 25% EtOAc in hexanes) to afford the title compound as a yellow-orange solid (1.2774 g, 3.488 mmol, 87%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.93 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.83 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.21 (d, *J* = 1.4 Hz, 1H), 7.07 (d, *J* = 1.3 Hz, 1H), 4.20 (s, 2H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 166.32, 161.76, 135.07, 133.57, 130.62, 128.94, 124.26, 123.28, 109.78, 32.13.

HRMS: (ESI-TOF) calculated for C₁₄H₉BrNO₄S⁺ ([M+H]⁺): 365.94392, found 365.94249.

FTIR (thin film, cm⁻¹): ν 3107 (w), 2893 (w), 1813 (m), 1786 (m), 1736 (s), 1609 (w), 1534 (w), 1467 (m), 1401 (m), 1359 (m), 1315 (m), 1289 (w), 1234 (w), 1185 (m), 1156 (m), 1144 (w), 1131 (m), 1067 (s), 1014 (m), 967 (s), 929 (m), 896 (m), 876 (s), 837 (m), 820 (m), 794 (s), 734 (s), 697 (s).

1,3-dioxoisindolin-2-yl 2-cyclopentyl-2-(4-(trifluoromethyl)phenyl)acetate (S12)

A 200-mL flask was charged with 2-(4-(trifluoromethyl)phenyl)acetic acid (4.1077 g, 20.12 mmol, 1 equiv.) followed by 40 mL of MeOH. Concentrated sulfuric acid (5 mL) was added slowly. The flask was fitted with a reflux condenser and heated at reflux overnight. After refluxing overnight, the reaction mixture was neutralized using saturated sodium carbonate. After neutralization, the reaction mixture was transferred to a separatory funnel and extracted 4 times with EtOAc. The combined organic extracts were dried over magnesium sulfate, filtered, and then concentrated via rotary evaporation to a slightly yellow oily residue. The residue was subjected to column chromatography using 15-25% EtOAc/hexanes. Methyl 2-(4-(trifluoromethyl)phenyl)acetate was obtained (3.9034 g, 17.89 mmol, 89%) as a slightly yellow oil.

¹H NMR (500 MHz, Chloroform-*d*): δ 7.59 (d, *J* = 8.1 Hz, 2H), 7.40 (d, *J* = 8.0 Hz, 2H), 3.71 (s, 3H), 3.69 (s, 2H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 171.37, 138.02, 129.83, 129.63 (q, *J* = 32.4 Hz), 125.66 (q, *J* = 3.7 Hz), 124.25 (q, *J* = 27.2 Hz), 52.41, 41.01.

¹⁹F NMR (376 MHz, Chloroform-*d*): δ -62.60 (s, 3F).

To an oven dried 50 mL flask was added KOtBu (1.1234 g, 10 mmol, 1.25 equiv.). The flask was placed under nitrogen and then charged with 15 mL of DMF and cooled to 0 °C. Methyl 2-cyclopentyl-2-(4-(trifluoromethyl)phenyl)acetate (1.7509 g, 8.03 mmol, 1 equiv.) was added as a solution in 4 mL of DMF. The reaction mixture turned orange-red as the solution was stirred for 40 minutes. Then cyclopentyl bromide (1.2 mL, 12 mmol, 1.5 equiv.) was added via syringe. Sodium bromide was observed to precipitate. After 3 hours, the reaction mixture was neutralized with saturated ammonium chloride and transferred to a separatory funnel. The organics were extracted with EtOAc 3 times and then were dried over magnesium sulfate and concentrated. The resulting oily residue was purified over silica with flash chromatography (3 to 5% EtOAc in hexanes) to afford methyl 2-cyclopentyl-2-(4-(trifluoromethyl)phenyl)acetate as an oil (2.0656 g, 7.125 mmol, 90%).

¹H NMR (400 MHz, Chloroform-*d*): δ 7.57 (d, *J* = 8.6 Hz, 2H), 7.46 (d, *J* = 8.1 Hz, 2H), 3.66 (s, 3H), 3.35 (d, *J* = 11.1 Hz, 1H), 2.55 (dt, *J* = 11.0, 8.8, 7.2 Hz, 1H), 2.00 – 1.83 (m, 1H), 1.74 – 1.55 (m, 3H), 1.53 – 1.36 (m, 2H), 1.27 (dq, *J* = 12.7, 8.4 Hz, 1H), 1.06 – 0.92 (m, 1H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 173.93, 143.06, 129.62 (q, *J* = 32.5 Hz), 128.77, 125.58 (q, *J* = 3.8 Hz), 124.29 (q, *J* = 272.0 Hz), 57.65, 52.16, 43.73, 31.64, 30.84, 25.19, 24.93.

¹⁹F NMR (376 MHz, Chloroform-*d*): δ -62.53 (s, 3F).

To a flask containing methyl 2-cyclopentyl-2-(4-(trifluoromethyl)phenyl)acetate (2.0656 g, 6.88 mmol, 1 equiv.) was added sodium hydroxide (1.01 g, 25 mmol, 3.67 equiv), 30 mL of MeOH and 5 mL of water. The flask was stirred overnight at room temperature. After stirring overnight, the reaction mixture was decanted to a separatory funnel and washed with ether. The ether wash was discarded. The aqueous layer was acidified using concentrated HCl to pH 2. After acidifying, the organics were extracted 4 times with ether. The organics were dried over magnesium sulfate and then concentrated via rotary evaporation and dried under vacuum to afford 2-cyclopentyl-2-(4-(trifluoromethyl)phenyl)acetic acid as a crystalline white solid (1.9217 g, 7.058 mmol, 98%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.58 (d, *J* = 8.1 Hz, 2H), 7.48 (d, *J* = 8.1 Hz, 2H), 3.36 (d, *J* = 11.1 Hz, 1H), 2.54 (dddd, *J* = 16.0, 11.2, 8.8, 7.3 Hz, 1H), 1.97 (dtd, *J* = 12.3, 7.4, 4.5 Hz, 1H), 1.74–1.66 (m, 1H), 1.66–1.55 (m, 2H), 1.53 – 1.38 (m, 2H), 1.33 (m, 1H), 0.98 (m, 1H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 178.93, 142.29, 129.75 (q, *J* = 32.5 Hz), 128.76, 125.53 (q, *J* = 3.7 Hz), 124.09 (q, *J* = 272.0 Hz), 57.43, 43.21, 31.50, 30.69, 25.08, 24.78.

¹⁹F NMR (376 MHz, Chloroform-*d*): δ -62.58 (s, 3F).

Synthesized according to general procedure A with 2-cyclopentyl-2-(4-(trifluoromethyl)phenyl)acetic acid (1.9217 g, 7 mmol, 1 equiv.), *N*-hydroxyphthalimide (1.7118 g, 10.5 mmol, 1.5 equiv.), DMAP (48.9 mg, 0.35 mmol, 0.05 equiv.) and DIC (0.87 mL, 5.58 mmol, 0.8 equiv.). Purified over silica with flash chromatography (5 to 25% EtOAc in hexanes) to afford the title compound as a white solid (2.7877 g, 6.68 mmol, 95%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.86 (dd, *J* = 5.6, 3.1 Hz, 2H), 7.78 (dd, *J* = 5.6, 3.1 Hz, 2H), 7.64 (d, *J* = 8.1 Hz, 2H), 7.54 (d, *J* = 8.0 Hz, 2H), 3.75 (d, *J* = 10.7 Hz, 1H), 2.67 – 2.52 (m, 1H), 2.18 – 2.09 (m, 1H), 1.82 – 1.71 (m, 1H), 1.71 – 1.60 (m, 2H), 1.58 – 1.47 (m, 3H), 1.18 – 1.06 (m, 1H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 169.69, 161.94, 140.82 (d, *J* = 1.4 Hz), 134.96, 130.28 (q, *J* = 32.6 Hz), 129.02, 128.90, 125.91 (q, *J* = 3.7 Hz), 124.17 (q, *J* = 272.0 Hz), 124.13, 54.42, 44.12, 31.48, 31.01, 25.22, 24.86.

¹⁹F NMR (282 MHz, Chloroform-*d*): δ -62.58 (s, 3F).

HRMS: (ESI-TOF) calculated for C₂₂H₁₉F₃NO₄⁺ ([M+H]⁺): 418.12607, found 418.12569.

FTIR (thin film, cm⁻¹): ν 2959 (w), 2879 (w), 1804 (w), 1780 (m), 1743 (s), 1619 (w), 1466 (w), 1454 (w), 1421 (w), 1354 (m), 1323 (s), 1290 (w), 1184 (m), 1164 (s), 1135 (s), 1120 (s), 1109 (s), 1081 (m), 1059 (s), 1019 (s), 966 (s), 906 (m), 873 (s), 836 (m), 787 (m), 724 (w), 694 (s), 658 (m), 636 (w), 603 (m), 517 (s), 495 (w), 401 (w).

1,3-dioxoisindolin-2-yl 2-(6-chloropyridin-3-yl)propanoate (S13)

2-(6-chloropyridin-3-yl)propanoic acid was prepared according to Liu, *et. al.*⁴ Prepared according to general procedure A with 2-(6-chloropyridin-3-yl)propanoic acid (2.275 g, 12.3 mmol, 1 equiv.), *N*-hydroxyphthalimide (1.5985 g, 9.8 mmol, 0.8 equiv.), DMAP (70.6 mg, 0.62 mmol, 0.05 equiv.) and DIC (2.2 mL, 14 mmol, 1.4 equiv.). Purified over silica with flash chromatography (30 to 50% EtOAc in hexanes) to afford the title compound as a white solid with some *N*-hydroxyphthalimide as an impurity. The solid was subjected to recrystallization from diethyl ether to afford the title compound (1.4539 g, 35.9%).

¹H NMR (500 MHz, Methylene Chloride-*d*₂): δ 8.43 (s, 1H), 7.95 – 7.72 (m, 5H), 7.38 (d, *J* = 8.9 Hz, 1H), 4.19 (q, *J* = 6.7, 6.1 Hz, 1H), 1.68 (d, *J* = 7.7 Hz, 3H).

¹³C NMR (126 MHz, Methylene Chloride-*d*₂): δ 170.64, 162.19, 151.35, 149.62, 138.51, 135.52, 133.81, 129.18, 124.97, 124.44, 40.46, 19.07.

HRMS: (ESI-TOF) calculated for C₁₆H₁₂ClN₂O₄S⁺ ([M+H]⁺): 331.04801, found 331.04770.

FTIR (thin film, cm⁻¹): ν 3515 (w), 2994 (w), 2360 (w), 2340 (w), 1810 (m), 1782 (s), 1737 (s), 1609 (m), 1585 (m), 1564 (m), 1457 (s), 1394 (m), 1356 (s), 1331 (m), 1289 (m), 1185 (s), 1169 (s), 1157 (m), 1138 (s), 1103 (s), 1080 (s), 1049 (s), 1024 (s), 1016 (s), 981 (s), 957 (s), 875 (s), 844 (s), 808 (m), 790 (s), 774 (s), 727 (m), 693 (s), 630 (m), 601 (m), 588 (m), 519 (s), 472 (m), 457 (m), 420 (m).

This matched literature characterization.⁴

1,3-dioxoisindolin-2-yl 4-(dimethylamino)-2-(naphthalen-2-yl)-4-oxobutanoate (S14)

A 50-mL oven-dried flask with a stir bar was placed under nitrogen. The flask was charged with diisopropylamine (1.4 mL, 9.9 mmol, 1.2 equiv.) and 10 mL of THF. The flask was cooled to -78 °C. *n*-BuLi (3.60 mL, 2.5 M in hexanes, 1.08 equiv.) was added via syringe. The reaction mixture was stirred for 10 minutes. Then, methyl 2-(naphthalene-2-yl)acetate (1.6613 g, 8.3 mmol, 1 equiv.) was added as a solution in 20 mL of THF. The reaction turned a fluorescent yellow/orange and was stirred for 15 minutes. Dimethyl bromoacetate (1.1 mL, 10 mmol, 1.2 equiv.) was then added via syringe and the reaction was allowed to stir overnight and warm to room temperature. The reaction mixture faded to a cream color as the reaction proceeded. The reaction mixture was quenched with saturated ammonium chloride. The organics were extracted 4 times with EtOAc. The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated via rotary evaporation to yield a cream solid. Purified over silica with flash chromatography (15 to 85% EtOAc in hexanes) to afford methyl 4-(dimethylamino)-2-(naphthalen-2-yl)-4-oxobutanoate was obtained as a white solid (2.1303 g, 7.47 mmol, 90%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.81 (d, *J* = 8.4 Hz, 3H), 7.76 (d, *J* = 1.8 Hz, 1H), 7.50 – 7.42 (m, 3H), 4.36 (dd, *J* = 10.7, 4.1 Hz, 1H), 3.69 (s, 3H), 3.35 (dd, *J* = 16.4, 10.7 Hz, 1H), 3.00 (s, 3H), 2.95 (s, 3H), 2.65 (dd, *J* = 16.4, 4.0 Hz, 1H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 174.29, 170.56, 135.95, 133.46, 132.68, 128.62, 127.82, 127.66, 126.61, 126.35, 126.03, 125.84, 52.37, 47.51, 37.76, 37.04, 35.49.

A 100-mL flask was charged with NaOH (1.05 g, 26 mmol, 3.5 equiv.) and methyl 4-(dimethylamino)-2-(naphthalen-2-yl)-4-oxobutanoate (2.1114 g, 7.4 mmol, 1 equiv.). The flask was charged with 40 mL of MeOH and 5 mL of water. The reaction mixture was stirred at room temperature overnight. The reaction mixture was acidified to pH 2 using conc. HCl. The organics were extracted 4 times with EtOAc. The organics were dried over magnesium sulfate, filtered, concentrated via rotary evaporation, and dried under vacuum to afford 4-(dimethylamino)-2-(naphthalen-2-yl)-4-oxobutanoic acid as a white solid (1.8017 g, 6.64 mmol, 90%).

¹H NMR (400 MHz, Chloroform-*d*): δ 7.85 – 7.78 (m, 4H), 7.52 – 7.43 (m, 3H), 4.40 (dd, J = 10.5, 3.8 Hz, 1H), 3.32 (dd, J = 16.5, 10.5 Hz, 1H), 2.99 (s, 3H), 2.92 (s, 3H), 2.72 (dd, J = 16.5, 3.8 Hz, 1H).

Prepared according to general procedure C with 4-(dimethylamino)-2-(naphthalen-2-yl)-4-oxobutanoic acid (1.3531 g, 5 mmol, 1 equiv.), *N*-hydroxyphthalimide (0.9019 g, 5.5 mmol, 1.1 equiv.), DMAP (33.6 mg, 0.25 mmol, 0.05 equiv.), EDC•HCl (1.0024 g, 5.25 mmol, 1.05 equiv.) and 25 mL THF. Purified over silica with flash chromatography (25 to 85% EtOAc in hexanes) to afford the title compound as a white solid (0.9696 g, 2.328 mmol, 73%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.94 – 7.82 (m, 6H), 7.75 (dd, J = 5.5, 3.1 Hz, 2H), 7.54 (dd, J = 8.5, 1.9 Hz, 1H), 7.51 – 7.48 (m, 2H), 4.82 (dd, J = 9.0, 5.3 Hz, 1H), 3.34 (dd, J = 16.4, 9.0 Hz, 1H), 2.97 (s, 3H), 2.96 (s, 3H), 2.91 (dd, J = 16.4, 5.4 Hz, 1H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 170.33, 169.32, 161.64, 134.64, 133.89, 133.51, 132.93, 129.00, 128.87, 128.07, 127.73, 127.33, 126.45, 126.31, 125.62, 123.91, 45.39, 37.96, 37.03, 35.64.

HRMS: (ESI-TOF) calculated for C₂₄H₂₁N₂O₅⁺ ([M+H]⁺): 417.14450, found 417.14362.

FTIR (thin film, cm⁻¹): ν 3048 (w), 2931 (w), 1802 (w), 1777 (m), 1738 (s), 1650 (s), 1549 (w), 1510 (w), 1500 (w), 1467 (m), 1453 (w), 1417 (w), 1400 (m), 1351 (m), 1292 (w), 1262 (w), 1238 (w), 1216 (w), 1205 (w), 1185 (m), 1159 (w), 1146 (w), 1122 (m), 1090 (m), 1049 (m), 1014 (w), 988 (m), 963 (m), 929 (w), 895 (w), 875 (m), 848 (m), 837 (m), 818 (m), 788 (m), 767 (w), 753 (m), 735 (w), 705 (m), 698 (s), 681 (w), 663 (m), 642 (m), 622 (w), 611 (w), 571 (w), 518 (m), 506 (m), 482 (m), 426 (w), 411 (w), 404 (w).

1,3-dioxoisindolin-2-yl 2-(4-(azidomethyl)phenyl)propanoate (S15)

Safety note: This procedure results in the production of hydrazoic acid which represents a potential explosion hazard. During workup and acidifying, it is important to use sufficient quantities of water to generate only dilute, aqueous solutions of hydrazoic acid and to be cognizant of the toxicity of HN₃.

According to Büll, *et. al.*⁵ a 50-mL oven-dried flask was charged with 2-(4-bromomethyl)phenyl)propionic acid (1.4673 g, 6 mmol, 1 equiv.) and sodium azide (0.6129 g, 9.4 mmol, 1.6 equiv.). The flask was placed under nitrogen and then charged with 25 mL of DMF. The reaction mixture was overnight at room temperature. After stirring the reaction was decanted to a separatory funnel, diluted with water and then with 1 N HCl and extracted 4 times using EtOAc. The combined organics were dried over magnesium sulfate, filtered, and concentrated via rotary evaporation. Purified over silica with flash chromatography (20 to 40% EtOAc in hexanes) to afford 2-(4-(azidomethyl)phenyl)propanoic acid as a slightly yellow solid (1.1951 g, 5.82 mmol, 96%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.35 (d, J = 8.2 Hz, 2H), 7.29 (d, J = 8.2 Hz, 2H), 4.33 (s, 2H), 3.76 (q, J = 7.2 Hz, 1H), 1.52 (d, J = 7.2 Hz, 3H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 178.94, 140.04, 134.79, 128.68, 128.25, 54.58, 44.98, 18.28.

Prepared according to general procedure A with 2-(4-(azidomethyl)phenyl)propanoic acid (1.1951 g, 5.8 mmol, 1 equiv.), *N*-hydroxyphthalimide (1.4517 g, 9 mmol, 1.5 equiv.), DMAP (35.8 mg, 0.3 mmol, 0.05 equiv.) and DIC (1.5 mL, 8.4 mmol, 1.4 equiv.). Purified over silica with flash chromatography (10 to 20% EtOAc in hexanes) to afford the title compound as a white solid (1.8688 g, 5.33 mmol, 92%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.87 (dd, J = 5.5, 3.1 Hz, 2H), 7.78 (dd, J = 5.5, 3.1 Hz, 2H), 7.43 (d, J = 8.2 Hz, 2H), 7.36 (d, J = 8.2 Hz, 2H), 4.36 (s, 2H), 4.14 (q, J = 7.2 Hz, 1H), 1.68 (d, J = 7.1 Hz, 3H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 170.75, 138.60, 135.22, 134.92, 129.05, 128.86, 128.24, 124.11, 54.57, 42.84, 19.09.

HRMS: (ESI-TOF) calculated for $C_{18}H_{15}N_2O_4^+$ ($[M+H-N_2]^+$): 323.10263, found 323.10241.

FTIR (thin film, cm^{-1}): ν 2981 (w), 2123 (w), 2089 (m), 2030 (w), 2017 (w), 1992 (w), 1967 (w), 1943 (w), 1918 (w), 1869 (w), 1844 (w), 1830 (w), 1802 (m), 1781 (m), 1741 (s), 1685 (w), 1653 (w), 1636 (w), 1606 (w), 1510 (w), 1467 (w), 1454 (w), 1437 (w), 1419 (w), 1358 (m), 1239 (m), 1213 (w), 1201 (w), 1186 (m), 1169 (m), 1124 (m), 1103 (m), 1080 (m), 1049 (s), 1021 (m), 1002 (m), 985 (w), 957 (m), 876 (s), 856 (m), 824 (w), 788 (w), 774 (m), 724 (m), 693 (s), 610 (w), 588 (w), 570 (m), 552 (w), 536 (w), 518 (m), 481 (w), 448 (w), 403 (w).

1,3-dioxoisindolin-2-yl 2-(3-benzoylphenyl)propanoate (S16)

Synthesized according to general procedure A with 2-(3-benzoylphenyl)propanoic acid (1.263 g, 5 mmol, 1 equiv.), *N*-hydroxyphthalimide (1.179 g, 7.5 mmol, 1.5 equiv.), DMAP (40.3 mg, 0.25 mmol, 0.05 equiv.) and DIC (950 μ L, 7 mmol, 1.4 equiv.). Purified over silica with flash chromatography (10 to 30% EtOAc in hexanes) to afford the title compound as a white solid (1.657 g, 4.15 mmol, 83%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.88 (dd, J = 5.5, 3.1 Hz, 2H), 7.87 – 7.83 (m, 3H), 7.79 (dt, J = 5.5, 3.1 Hz, 2H), 7.77 (dt, J = 7.7, 1.4 Hz, 1H), 7.67 (dt, J = 7.7, 1.5 Hz, 1H), 7.60 (tt, 7.5, 1.3 Hz, 1H), 7.53 (t, J = 7.8 Hz, 1H), 7.50 (t, J = 7.7 Hz, 2H), 4.20 (q, J = 7.2 Hz, 1H), 1.71 (d, J = 7.1 Hz, 3H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 196.44, 170.57, 138.74, 138.39, 137.47, 134.95, 132.72, 131.67, 130.35, 129.79, 129.46, 129.13, 129.05, 128.52, 124.13, 43.00, 19.04. (1 carbon peak obscured by overlap)

HRMS: (ESI-TOF) calculated for $C_{24}H_{18}NO_5^+$ ($[M+H]^+$): 400.11795, found 400.11798.

FTIR (thin film, cm^{-1}): ν 3488 (w), 3382 (w), 3064 (w), 2926 (w), 1811 (w), 1783 (m), 1735 (s), 1646 (m), 1621 (m), 1597 (m), 1488 (w), 1469 (m), 1447 (m), 1437 (m), 1365 (m), 1350 (m), 1313 (m), 1284 (s), 1258 (m), 1232 (m), 1185 (s), 1122 (s), 1080 (s), 1045 (s), 1014 (m), 993 (s), 971 (s), 954 (s), 924 (m), 876 (s), 853 (s), 820 (s), 804 (m), 792 (m), 783 (m), 777 (m), 753 (m), 722 (m), 709 (s), 694 (s), 687 (s).

1,3-dioxoisindolin-2-yl 2-methyl-2-phenylpropanoate (S17)

Prepared according to general procedure A with 2-phenylisobutyric acid (1.6978 g, 10.4 mmol, 1 equiv.), *N*-hydroxyphthalimide (2.380 g, 15 mmol, 1.5 equiv.), DMAP (66.3 mg, 0.5 mmol, 0.05 equiv.) and DIC (2.0 mL, 14 mmol, 1.4 equiv.). Purified over silica with flash chromatography (10 to 30% EtOAc in hexanes) to afford the title compound (2.7783 g, 8.98 mmol, 87%)

¹H NMR (500 MHz, Chloroform-*d*): δ 7.87 (dd, $J = 5.5, 3.1$ Hz, 1H), 7.78 (dd, $J = 5.5, 3.1$ Hz, 1H), 7.51 – 7.49 (m, 1H), 7.42 (dd, $J = 8.6, 7.0$ Hz, 1H), 7.34 – 7.30 (m, 1H), 1.79 (s, 6H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 173.37, 162.10, 142.71, 134.83, 129.15, 128.81, 127.57, 125.93, 124.02, 46.49, 26.99.

HRMS: (ESI-TOF) calculated for $C_{18}H_{16}NO_4^+$ ($[M+H]^+$): 310.10738, found 310.1075.

FTIR (thin film, cm⁻¹): ν 3060 (w), 3006 (w), 2977 (w), 2934 (w), 1803 (w), 1772 (s), 1740 (s), 1599 (w), 1494 (w), 1469 (m), 1447 (w), 1392 (w), 1369 (m), 1358 (m), 1332 (w), 1295 (w), 1234 (w), 1220 (w), 1187 (s), 1159 (w), 1132 (m), 1109 (m), 1081 (w), 1055 (s), 1030 (m), 1017 (m), 1008 (s), 965 (s), 947 (m), 931 (m), 915 (w), 874 (s), 850 (s), 788 (s), 775 (s), 725 (s), 696 (s), 599 (s), 543 (m), 517 (s), 484 (m), 419 (m).

1,3-dioxoisindolin-2-yl 1-(4-chlorophenyl)cyclohexane-1-carboxylate (S18)

Prepared according to general procedure A with 1-(4-chlorophenyl)cyclohexane-1-carboxylic acid (1.1887 g, 5.00 mmol, 1 equiv.), *N*-hydroxyphthalimide (1.2407 g, 7.50 mmol, 1.5 equiv.), DMAP (30.7 mg, 0.25 mmol, 0.05 equiv.) and DIC (1.1 mL, 7 mmol, 1.4 equiv.). Purified over silica with flash chromatography (5 to 25% EtOAc in hexanes) to afford the title compound (1.7094 g, 4.45 mmol, 89%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.86 (dd, $J = 5.6, 3.1$ Hz, 2H), 7.78 (dd, $J = 5.6, 3.1$ Hz, 2H), 7.46 (d, $J = 8.1$ Hz, 2H), 7.39 (d, $J = 8.4$ Hz, 2H), 2.61 (d, $J = 12.9$ Hz, 2H), 1.79 (m, 7H), 1.33 (d, $J = 12.9$ Hz, 1H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 171.47, 162.17, 140.77, 134.88, 133.61, 129.13, 129.02, 127.64, 124.03, 50.83, 35.40, 25.44, 23.48.

HRMS: (ESI-TOF) calculated for $C_{21}H_{19}Cl^{35}NO_4^+$ ($[M+H]^+$): 384.09971, found 384.09910.

(ESI-TOF) calculated for $C_{21}H_{19}Cl^{37}NO_4^+$ ($[M+H]^+$): 386.09763, found 386.09678.

FTIR (thin film, cm⁻¹): ν 2932 (w), 2864 (w), 1806 (w), 1783 (m), 1740 (s), 1591 (w), 1492 (m), 1467 (m), 1457 (w), 1402 (w), 1373 (m), 1356 (m), 1282 (w), 1186 (m), 1169 (m), 1125 (m), 1092 (m), 1074 (m), 1057 (s), 1033 (s), 1009 (m), 971 (s), 924 (m), 908 (m), 897 (m), 874 (s), 845 (m), 827 (s), 787 (m), 745 (m), 717 (m), 697 (s), 611 (w), 571 (w), 538 (w), 519 (s), 461 (w), 443 (m).

1,3-dioxoisindolin-2-yl 1-(4-chlorophenyl)cyclopentane-1-carboxylate (S19)

Prepared according to general procedure A with 1-(4-chlorophenyl)cyclopentane-1-carboxylic acid (1.1270 g, 5 mmol, 1 equiv.), *N*-hydroxyphthalimide (1.2052 g, 7.5 mmol, 1.5 equiv.), DMAP (32.2 mg, 0.25 mmol, 0.05 equiv.) and DIC (1.1 mL, 7 mmol, 1.4 equiv.). Purified over silica with flash chromatography (5 to 25% EtOAc in hexanes) to afford the title compound (1.7766 g, 4.80 mmol, 96%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.85 (dd, $J = 5.5, 3.1$ Hz, 2H), 7.77 (dd, $J = 5.5, 3.0$ Hz, 2H), 7.42 (d, $J = 8.7$ Hz, 2H), 7.37 (d, $J = 8.7$ Hz, 2H), 2.80 – 2.74 (m, 2H), 2.12 – 2.05 (m, 2H), 1.97 – 1.81 (m, 4H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 172.35, 162.09, 139.77, 134.87, 133.55, 129.10, 128.91, 128.40, 124.02, 57.68, 37.25, 23.89.

HRMS: (ESI-TOF) calculated for $C_{20}H_{16}Cl^{35}NNaO_4^+$ ($[M+Na]^+$): 392.06601, found 392.06581.

(ESI-TOF) calculated for $C_{20}H_{16}Cl^{37}NNaO_4^+$ ($[M+Na]^+$): 394.06387, found 394.06230.

FTIR (thin film, cm⁻¹): ν 2977 (w), 2875 (w), 1803 (m), 1781 (m), 1737 (s), 1609 (w), 1490 (m), 1466 (m), 1453 (m), 1402 (w), 1361 (m), 1300 (w), 1186 (m), 1170 (w), 1133 (m), 1104 (w), 1068 (s), 1031 (m), 1014 (m), 982 (s), 966 (m), 952 (m), 895 (w), 874 (s), 829 (s), 785 (s), 749 (m), 717 (m), 696 (s), 632 (w), 607 (m), 584 (m), 515 (s), 481 (m), 441 (m), 404 (m).

1,3-dioxoisindolin-2-yl 1-(4-chlorophenyl)cyclobutane-1-carboxylate (S20)

Prepared according to general procedure A with 1-(4-chlorophenyl)cyclobutane-1-carboxylic acid (1.0394 g, 5 mmol, 1 equiv.), *N*-hydroxyphthalimide (1.2175 g, 7.5 mmol, 1.5 equiv.), DMAP (31.4 mg, 0.25 mmol, 0.05 equiv.) and DIC (1.1 mL, 7 mmol, 1.4 equiv.). Purified over silica with flash chromatography (10 to 25% EtOAc in hexanes) to afford the title compound (1.6953 g, 4.77 mmol, 97%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.86 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.77 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.40 – 7.35 (m, 4H), 3.06 (tdd, *J* = 9.0, 6.2, 3.8 Hz, 2H), 2.65 (tdd, *J* = 9.3, 7.8, 2.8 Hz, 2H), 2.26 (dddd, *J* = 16.8, 11.5, 9.1, 7.8 Hz, 1H), 2.02 (dt, *J* = 11.6, 9.2, 5.2 Hz, 1H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 171.96, 162.05, 139.80, 134.88, 133.51, 129.11, 128.97, 128.04, 124.05, 50.61, 32.81, 16.86

HRMS: (ESI-TOF) calculated for C₁₉H₁₄Cl³⁵NNaO₄⁺ (*[M*+Na]⁺): 378.05036, found 378.05014.

(ESI-TOF) calculated for C₁₉H₁₄Cl³⁷NNaO₄⁺ (*[M*+Na]⁺): 380.04816, found 380.04645.

FTIR (thin film, cm⁻¹): ν 2947 (w), 1802 (w), 1773 (s), 1737 (s), 1492 (m), 1466 (m), 1400 (w), 1367 (m), 1247 (w), 1184 (m), 1169 (s), 1125 (m), 1112 (m), 1093 (m), 1074 (s), 1053 (m), 1021 (s), 1010 (s), 959 (s), 874 (s), 833 (s), 776 (m), 719 (m), 709 (m), 692 (s), 598 (m), 536 (m), 516 (s), 493 (m), 435 (m), 407 (m).

1,3-dioxoisindolin-2-yl 4-(6-chloropyridin-3-yl)tetrahydro-2H-pyran-4-carboxylate (S21)

To a 100-mL flask with a stir bar was added 6-chloro-3-pyridineacetic acid (1.127 g, 6.6 mmol, 1 equiv). Then, 15 mL ethanol and 1.6 mL sulfuric acid were added. A reflux condenser was then attached to the flask and the flask was heated in an oil bath at 95°C until reflux was observed. The reaction was left stirring for 16 hours overnight, then cooled to room temperature. Then the reaction mixture was poured into a separatory funnel, diluted with 30 mL diethyl ether and washed 2 times with NaHCO₃ (2 x 15 mL). The organic layer was then washed with brine and dried over sodium sulfate. Concentration under vacuum afforded a brown oil which was purified over silica with flash chromatography (15 to 30% EtOAc in hexanes) to afford ethyl 2-(6-chloropyridin-3-yl)acetate (0.999 g, 5.00 mmol, 76%) as a colorless oil.

¹H NMR (500 MHz, Chloroform-*d*): δ 8.29 (dd, *J* = 2.5, 0.8 Hz, 1H), 7.62 (dd, *J* = 8.2, 2.5 Hz, 1H), 7.30 (dd, *J* = 8.2, 0.7 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.60 (s, 2H), 1.26 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 170.39, 150.47, 150.23, 139.83, 128.88, 124.22, 61.53, 37.77, 14.26.

HRMS: (EI) calculated for C₉H₁₀ClNO₂⁺ (*[M**]⁺): 199.03946, found 199.03954.

FTIR (thin film, cm⁻¹): ν 2982 (w), 1729 (s), 1588 (w), 1567 (w), 1460 (s), 1417 (w), 1385 (m), 1368 (w), 1334 (w), 1290 (w), 1229 (m), 1159 (s), 1139 (s), 1101 (s), 1023 (s), 945 (w), 879 (w), 818 (m), 747 (w), 671 (w), 632 (w), 579 (w), 506 (w), 453 (w), 414 (w).

To a flame-dried 100-mL flask with a stir bar under N₂ was added LiHMDS (11.0 mL of a 1.0 M solution in THF, 11.0 mmol, 2.2 equiv.). The flask was placed into a dry ice/acetone bath and 30 mL of THF was added. In a separate vial with a septa cap under N₂ was added ethyl 2-(6-chloropyridin-3-yl)acetate (0.917 g, 5 mmol, 1 equiv.) and bis(2-bromoethyl)ether (910 μ L, 7.5 mmol, 1.5 equiv.). These were dissolved in 5 mL of anhydrous THF and added dropwise to the LiHMDS solution over 20 minutes with vigorous stirring. The vial was rinsed with an additional 10 mL of THF and the yellow reaction was allowed to stir and warm up to room temperature overnight. The red reaction mixture was poured into a separatory funnel and quenched with saturated NH₄Cl. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were rinsed with brine, dried over Na₂SO₄ and concentrated

under vacuum. The crude oil was purified over silica with flash chromatography (40 to 80% EtOAc in hexanes) to afford a light yellow oil (1.1805 g, 4.38 mmol, 95% yield).

¹H NMR (500 MHz, Chloroform-*d*): δ 8.41 (d, *J* = 2.7 Hz, 1H), 7.65 (dd, *J* = 8.5, 2.7 Hz, 1H), 7.31 (dd, *J* = 8.4, 0.7 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.94 (dt, *J* = 12.1, 3.8 Hz, 2H), 3.56 (td, *J* = 11.7, 2.0 Hz, 2H), 2.53 (dd, *J* = 13.7, 2.6 Hz, 2H), 1.95 (ddd, *J* = 13.4, 11.2, 4.4 Hz, 2H), 1.20 (t, *J* = 7.1 Hz, 3H).

HRMS: (ESI-TOF) calculated for C₁₃H₁₆ClNO⁺ ([M+H]⁺): 270.08915, found 270.0892.

FTIR (thin film, cm⁻¹): ν 2962 (w), 2934 (w), 2854 (w), 1724 (s), 1581 (w), 1562 (w), 1463 (m), 1389 (w), 1370 (w), 1294 (m), 1220 (m), 1195 (s), 1129 (s), 1103 (s), 1047 (m), 1019 (s), 947 (w), 915 (w), 860 (w), 836 (w), 813 (w), 768 (w), 742 (m), 633 (w), 558 (w), 450 (w), 412 (w).

To an oven-dried 50-mL round bottom flask with a stir bar was added ethyl 4-(6-chloropyridin-3-yl)tetrahydro-2H-pyran-4-carboxylate (1.179g, 4.4 mmol, 1 equiv.) and 20 mL methanol. The mixture was stirred and 5 mL of a 6 M NaOH solution was added in one portion. Then, 1 mL water was added, and the reaction was stirred and monitored by TLC. After 16 hours, the reaction was concentrated under reduced pressure to a crude oil and then acidified with 6 M HCl until the mixture was pH 1. The mixture was then transferred to a separatory funnel and diluted with ether. The aqueous layer was washed with ether (2 x 50 mL) and the combined organic layers were washed with water and brine and dried over Na₂SO₄. The ether was then evaporated under reduced pressure to yield a crude white solid which was purified by column chromatography (30 to 60% EtOAc in hexanes) to afford the title compound as a white solid (0.8031 g, 3.32 mmol, 76%).

¹H NMR (500 MHz, Chloroform-*d*): δ 8.49 (dd, *J* = 2.7, 0.8 Hz, 1H), 7.73 (dd, *J* = 8.5, 2.7 Hz, 1H), 7.37 (dd, *J* = 8.4, 0.7 Hz, 1H), 3.98 (d, *J* = 12.1 Hz, 2H), 3.66 (ddd, *J* = 12.3, 11.1, 2.1 Hz, 2H), 2.58 (dd, *J* = 13.7, 2.7 Hz, 1H), 2.02 (ddd, *J* = 13.5, 11.1, 4.3 Hz, 2H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 176.72, 150.94, 147.88, 136.85, 136.55, 124.51, 65.31, 46.87, 33.81.

HRMS: (ESI-TOF) calculated for C₁₁H₁₂ClNO₃⁺ ([M+H]⁺): 242.05785, found 242.0577.

FTIR (thin film, cm⁻¹): ν 2967 (w), 2923 (w), 2847 (w), 2629 (w), 1688 (m), 1579 (w), 1565 (w), 1460 (w), 1443 (w), 1428 (w), 1401 (w), 1392 (w), 1374 (w), 1351 (w), 1298 (m), 1260 (w), 1246 (m), 1236 (m), 1203 (m), 1160 (w), 1136 (m), 1101 (s), 1047 (w), 1036 (w), 1020 (m), 954 (w), 938 (w), 911 (m), 895 (m), 850 (w), 827 (m), 772 (m), 759 (w), 739 (m), 687 (w), 632 (w), 582 (w), 551 (m), 511 (w), 466 (w), 448 (m), 413 (m).

Synthesized according to general procedure A with 4-(6-chloropyridin-3-yl)tetrahydro-2H-pyran-4-carboxylic acid (0.738 g, 3 mmol, 1 equiv.), *N*-hydroxyphthalimide (743.7 mg, 4.5 mmol, 1.5 equiv.), DMAP (32.1 mg, 0.15 mmol, 0.05 equiv) and DIC (650 μ L, 4.2 mmol, 1.4 equiv). Purified over silica with flash chromatography (15 to 60% EtOAc in hexanes) to afford the title compound as a white solid (0.2774 g, 0.717 mmol, 23%).

¹H NMR (400 MHz, Chloroform-*d*): δ 8.55 (dd, *J* = 2.8, 0.8 Hz, 1H), 7.88 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.85 – 7.77 (m, 3H), 7.42 (dd, *J* = 8.5, 0.8 Hz, 1H), 4.07 (ddd, *J* = 12.3, 4.4, 2.7 Hz, 2H), 3.83 (td, *J* = 11.8, 1.9 Hz, 1H), 2.65 (dd, *J* = 13.7, 2.3 Hz, 2H), 2.18 (ddd, *J* = 13.6, 11.5, 4.5 Hz, 2H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 170.19, 161.84, 151.42, 147.52, 136.94, 135.64, 135.13, 128.92, 124.67, 124.25, 77.16, 65.14, 47.46, 34.61.

HRMS: (ESI-TOF) calculated for C₁₉H₁₆ClNO₅⁺ ([M+H]⁺): 387.07423, found 387.0747.

FTIR (thin film, cm⁻¹): ν 3057 (w), 2967 (w), 2934 (w), 2864 (w), 1801 (w), 1775 (m), 1737 (s), 1605 (w), 1584 (w), 1563 (w), 1469 (m), 1436 (w), 1428 (w), 1392 (w), 1353 (m), 1328 (w), 1294 (w), 1245 (w), 1222 (w), 1185 (m), 1154 (w), 1141 (m), 1104 (s), 1073 (s), 1029 (s), 1017 (s), 963 (m), 930 (m), 914 (w), 889 (w), 873 (m), 850 (m), 841 (s), 812 (w), 784 (m), 755 (s), 739 (m), 695 (s), 635 (m), 607 (m), 582 (m), 552 (m), 536 (w), 516 (s), 478 (w), 449 (m), 436 (m), 412 (m), 403 (m).

1,3-dioxoisindolin-2-yl-adamantane-1-carboxylate (S22)

Synthesized according to general procedure A with 1-adamantanecarboxylic acid (0.9711 g, 5.3 mmol, 1 equiv.), *N*-hydroxyphthalimide (1.230 g, 7.5 mmol, 1.5 equiv), DMAP (45.7 mg, 0.3 mmol, 0.05 equiv) and DIC (1.1 mL, 8.4 mmol, 1.4 equiv). Purified over silica with flash chromatography (10 to 30% EtOAc in hexanes) to afford the title compound as a white solid (1.4662 g, 4.51 mmol, 84%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.88 (dd, J = 5.5, 3.1 Hz, 2H), 7.78 (dd, J = 5.5, 3.1 Hz, 2H), 2.14 (d, J = 3.0 Hz, 6H), 2.12 – 2.09 (t, J = 3.1 Hz 3H), 1.78 (t, J = 3.1 Hz, 6H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 173.41, 162.31, 134.76, 129.21, 123.99, 40.65, 38.58, 36.33, 27.77.

This matches previous literature characterization.⁶

1,3-dioxoisindolin-2-yl 3-(4-(tert-butyl)phenyl)-2,2-dimethylpropanoate (S23)

To an oven-dried 50-mL flask under nitrogen was added diisopropylamine (1.25 mL, 9 mmol, 1.1 equiv.) and 10 mL of THF. The flask was cooled to -78 °C and then charged with *n*-BuLi in hexanes (3.35 mL of a 2.5 M solution, 8.4 mmol, 1.05 equiv.). The reaction mixture was stirred for 5 minutes to generate LDA. Subsequently, methyl isobutyrate (0.92 mL, 8 mmol, 1 equiv.) was added via syringe. The reaction mixture was stirred for 20 minutes to generate the enolate at -78 °C. 1-(bromomethyl)-4-(tert-butyl)benzene (1.65 mL, 9 mmol, 1.13 equiv) was added in 10 mL of THF. The reaction mixture was stirred overnight and allowed to warm to room temperature. After quenching with saturated ammonium chloride, the reaction mixture was extracted 4 times with ethyl acetate. The combined organics were dried over sodium sulfate and concentrated via rotary evaporation resulting in a yellow, oily residue. The resulting ester was carried on without further characterization.

To the flask containing the crude methyl 3-(4-(tert-butyl)phenyl)-2,2-dimethylpropanoate was added sodium hydroxide (1.1 g, 27.5 mmol, 3.43 equiv.) as well as 5 mL of water and 30 mL of MeOH. The reaction mixture was stirred for 24 h at room temperature. Afterwards the reaction mixture was washed with ether and the ether wash was discarded. The reaction mixture was acidified to pH 2 using conc. HCl. The reaction mixture was then extracted 3 times using ether. The organics were combined, dried over sodium sulfate, and concentrated via rotary evaporation to yield 3-(4-(tert-butyl)phenyl)-2,2-dimethylpropanoic acid as a white solid (1.4434 g, 6.16 mmol, 77% over 2 steps).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.29 (d, J = 7.5 Hz, 2H), 7.10 (d, J = 7.8 Hz, 2H), 2.87 (s, 2H), 1.31 (s, 9H), 1.21 (s, 6H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 183.58, 149.42, 134.57, 130.08, 125.07, 45.43, 43.49, 34.52, 31.53, 24.83.

Synthesized according to general procedure A with 3-(4-*tert*-butylphenyl)-2,2-dimethylpropanoic acid (1.4434 g, 6 mmol, 1 equiv.), *N*-hydroxyphthalimide (1.5108 g, 9.3 mmol, 1.5 equiv.), DMAP (42.2 mg, 0.3 mmol, 0.05 equiv.) and DIC (1.35 mL, 8.4 mmol, 1.4 equiv.). Purified over silica with flash chromatography (15 to 25% EtOAc in hexanes) to afford the title compound as a white solid (2.1696 g, 5.72 mmol, 93%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.90 (dd, J = 5.5, 3.1 Hz, 2H), 7.80 (dd, J = 5.5, 3.1 Hz, 2H), 7.34 (d, J = 8.3 Hz, 2H), 7.24 (d, J = 8.2 Hz, 2H), 3.06 (s, 2H), 1.38 (s, 6H), 1.31 (s, 9H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 173.94, 162.26, 149.71, 134.83, 133.52, 130.25, 129.21, 125.25, 124.04, 45.23, 43.28, 34.57, 31.53, 25.01.

HRMS: (ESI-TOF) calculated for C₂₃H₂₆NO₄⁺ ([M+H]⁺): 380.18563, found 380.18575.

FTIR (thin film, cm⁻¹): ν 2960 (w), 2861 (w), 1807 (w), 1781 (m), 1739 (s), 1607 (w), 1519 (w), 1463 (m), 1450 (w), 1383 (m), 1358 (m), 1300 (w), 1269 (w), 1184 (m), 1168 (w), 1147 (m), 1134 (m), 1079 (m), 1054 (s), 1006 (m), 977 (m), 957 (m), 942 (m), 900 (w), 879 (s), 864 (w), 842 (m), 802 (m), 781 (m), 755 (w), 708 (m), 693 (s), 645 (w), 627 (m), 591 (m), 562 (m), 531 (w), 516 (m), 449 (w).

1,3-dioxoisindolin-2-yl 3-(4-cyanophenyl)-2,2-dimethylpropanoate (S24)

To an oven-dried 50-mL flask under nitrogen was added diisopropylamine (1.25 mL, 9.00 mmol, 1.1 equiv.) and 10 mL of THF. The flask was cooled to -78 °C and then charged with *n*-BuLi in hexanes (3.35 mL of a 2.5 M solution, 8.4 mmol, 1.05 equiv.). The reaction mixture was stirred for 5 minutes to generate LDA. Subsequently, methyl isobutyrate (0.93 mL, 8 mmol, 1 equiv.) was added via syringe. The reaction mixture was stirred for 20 minutes to generate the enolate at -78 °C. 4-(bromomethyl)benzonitrile (1.765 g, 9 mmol, 1.13 equiv.) was added in 10 mL of THF. The reaction mixture was stirred overnight and allowed to warm to room temperature. After quenching with saturated ammonium chloride, the reaction mixture was extracted 4 times with ethyl acetate. The combined organics were dried over sodium sulfate and concentrated via rotary evaporation resulting in a yellow, oily residue. The resulting ester was carried on without further characterization.

To the flask containing the crude methyl 3-(4-cyanophenyl)-2,2-dimethylpropanoate was added sodium hydroxide (0.97 g, 24.3 mmol, 3.0 equiv.) as well as 5 mL of water and 30 mL of MeOH. The reaction mixture was stirred for 24 h at room temperature. Afterwards the reaction mixture was washed with ether and the ether wash was discarded. The reaction mixture was acidified to pH 2 using conc. HCl. The reaction mixture was then extracted 3 times using ether. The organics were combined, dried over sodium sulfate, and concentrated via rotary evaporation to yield 3-(4-cyanophenyl)-2,2-dimethylpropanoic acid as a white solid (1.2108 g, 5.96 mmol, 75% over 2 steps).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.57 (d, J = 7.8 Hz, 2H), 7.28 (d, 8.3 Hz, 2H), 2.95 (s, 2H), 1.22 (s, 6H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 182.47, 143.32, 132.03, 131.14, 119.01, 110.80, 45.87, 43.51, 24.97.

Synthesized according to general procedure A with 3-(4-cyanophenyl)-2,2-dimethylpropanoic acid (1.2108 g, 6 mmol, 1 equiv.), *N*-hydroxyphthalimide (1.4579 g, 9.3 mmol, 1.5 equiv.), DMAP (40.3 mg, 0.3 mmol, 0.05 equiv.) and DIC (1.3 mL, 8.4 mmol, 1.4 equiv.). Purified over silica with flash chromatography (10 to 25% EtOAc in hexanes) to afford the title compound as a white solid (1.9452 g, 5.58 mmol, 94%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.90 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.81 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.63 (d, *J* = 8.1 Hz, 2H), 7.45 (d, *J* = 8.0 Hz, 2H), 3.13 (s, 2H), 1.40 (s, 6H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 173.10, 162.14, 142.19, 134.98, 132.24, 131.30, 129.07, 124.14, 119.04, 111.11, 46.03, 43.34, 25.27.

HRMS: (ESI-TOF) calculated for C₂₀H₁₇N₂O₅⁺ ([M+H]⁺): 349.11828, found 349.11746.

FTIR (thin film, cm⁻¹): ν 2992 (w), 2227 (w), 1803 (m), 1779 (m), 1738 (s), 1608 (w), 1509 (w), 1465 (m), 1417 (w), 1390 (w), 1371 (m), 1357 (m), 1286 (w), 1184 (m), 1132 (m), 1080 (m), 1042 (s), 1013 (s), 978 (m), 963 (m), 946 (w), 902 (w), 877 (s), 867 (m), 844 (m), 828 (m), 803 (m), 785 (m), 758 (w), 732 (w), 710 (w), 690 (s), 648 (w), 625 (w), 588 (m), 555 (m), 530 (w), 516 (m), 444 (w).

1,3-dioxoisindolin-2-yl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (41)

Synthesized according to general procedure A with 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoic acid (1.0135 g, 4.0 mmol, 1 equiv.), *N*-hydroxyphthalimide (0.9755 g, 6.0 mmol, 1.5 equiv.), DMAP (21.3mg, 0.2 mmol, 0.05 equiv.) and DIC (0.87 mL, 5.6 mmol, 1.4 equiv.). Purified over silica with flash chromatography (10 to 30% EtOAc in hexanes) to afford the title compound as a white solid (1.5616 g, 3.95 mmol, 98%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.89 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.79 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.00 (d, *J* = 7.3 Hz, 1H), 6.66 (m, 2H), 4.01 (t, *J* = 4.9 Hz, 2H), 2.31 (s, 3H), 2.19 (s, 3H), 2.00 – 1.91 (m, 4H), 1.45 (s, 6H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 173.79, 162.12, 156.97, 136.50, 134.70, 130.27, 129.07, 123.90, 123.62, 120.69, 111.99, 67.73, 41.98, 37.41, 25.15, 25.00, 21.42, 15.81.

HRMS: (ESI-TOF) calculated for C₂₃H₂₅NNaO₅⁺ ([M+Na]⁺): 418.16249, found 418.16148.

FTIR (thin film, cm⁻¹): ν 3004 (w), 2875 (w), 1849 (w), 1804 (m), 1778 (s), 1740 (s), 1616 (m), 1585 (m), 1510 (m), 1469 (m), 1414 (m), 1397 (m), 1373 (m), 1312 (m), 1276 (m), 1264 (s), 1210 (m), 1187 (m), 1158 (m), 1130 (s), 1080 (m), 1038 (s), 1000 (m), 969 (s), 947 (m), 931 (m), 877 (s), 856 (m), 837 (m), 813 (m), 803 (s), 786 (s), 766 (m), 754 (m), 704 (s), 693 (s).

1,3-dioxoisindolin-2-yl (2S,4aS,6aS,6bR,12aS,12bR,14bR)-2,4a,6a,6b,9,9,12a-heptamethyl-10,13-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-icosahydricene-2-carboxylate (S25)

Enoxolone was oxidized according to the procedure from Subba Rao, *et. al.*⁷ To a 500-mL round bottom flask with a stir bar was added 2.38 g enoxolone (2.38 g, 5 mmol, 1 equiv.) and 100 mL dry acetone. The flask was cooled to 0°C and Jones Reagent (3.0 mL of 2 M solution, Sigma, 6 mmol, 1.2 equiv) was added over 5 minutes until the brown color persisted. The mixture was stirred further for 40 minutes. 2-Propanol (8 mL) was then added to quench the reaction and the reaction mixture was filtered over a frit and the filtered solids were washed thoroughly with dichloromethane. The filtrate was concentrated to a viscous oil and then diluted to 200 mL with dichloromethane and poured into a separatory funnel. The organic layer was washed with water (2 x 100 mL), brine and then dried with

sodium sulfate. The solution was concentrated to yield an off-white solid which was used directly for phthalimide ester synthesis.

¹H NMR (500 MHz, Chloroform-*d*): δ 5.75 (s, 1H), 2.96 (dq, J = 11.0, 4.0, 3.5 Hz, 1H), 2.64 (ddd, J = 15.7, 11.3, 7.1 Hz, 1H), 2.45 (s, 1H), 2.36 (ddd, J = 15.8, 6.5, 4.0 Hz, 1H), 2.21 (dd, J = 13.3, 2.3 Hz, 1H), 2.09 – 1.98 (m, 2H), 1.94 (ddd, J = 13.7, 4.4, 2.7 Hz, 1H), 1.86 (td, J = 13.6, 4.6 Hz, 1H), 1.70 (td, J = 12.1, 5.5 Hz, 1H), 1.63 (t, J = 13.5 Hz, 1H), 1.60 – 1.50 (m, 1H), 1.44 (ddt, J = 18.0, 14.5, 7.2 Hz, 3H), 1.38 (s, 3H), 1.36 – 1.29 (m, 2H), 1.27 (s, 3H), 1.23 (s, 3H), 1.22 – 1.19 (m, 1H), 1.17 (s, 3H), 1.10 (s, 3H), 1.07 (s, 3H), 1.05 – 1.03 (m, 1H), 0.86 (s, 3H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 217.40, 199.82, 181.35, 169.94, 128.57, 61.20, 55.59, 48.39, 47.94, 45.43, 43.93, 43.46, 41.06, 39.88, 37.83, 36.85, 34.39, 32.27, 32.03, 31.05, 28.72, 28.57, 26.67, 26.52, 23.50, 21.60, 18.93, 18.68, 15.80.

HRMS: (ESI-TOF) calculated for C₃₀H₄₅O₄⁺ ([M+H]⁺): 469.33124, found 469.3317.

FTIR (thin film, cm⁻¹): ν 3305 (w), 2964 (w), 2947 (w), 2873 (w), 2848 (w), 2360 (w), 2340 (w), 2185 (w), 2050 (w), 2026 (w), 1978 (w), 1726 (s), 1681 (m), 1643 (s), 1617 (w), 1444 (w), 1385 (m), 1362 (w), 1347 (w), 1328 (w), 1279 (w), 1250 (w), 1205 (m), 1193 (w), 1175 (w), 1142 (m), 1110 (w), 1086 (m), 1071 (w), 1049 (w), 1028 (w), 989 (w), 982 (w), 948 (w), 885 (w), 873 (w), 822 (w), 779 (m), 747 (w), 727 (w), 692 (w), 669 (m), 622 (w), 605 (w), 584 (m), 560 (w), 537 (w), 479 (w), 461 (w), 418 (w), 403 (w).

Synthesized according to general procedure A with the acid from the previous step (0.9062 g, 1.9 mmol, 1 equiv.), *N*-hydroxyphthalimide (0.469 g, 3 mmol, 1.5 equiv.), DMAP (16.9 mg, 0.1 mmol, 0.05 equiv.) and DIC (0.5 mL, 2.7 mmol, 1.4 equiv.). Purified over silica with flash chromatography (10 to 30% EtOAc in hexanes) to afford the title compound as a white solid (1.1255 g, 1.83 mmol, 95%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.88 (dd, J = 5.4, 3.1 Hz, 2H), 7.79 (dd, J = 5.5, 3.1 Hz, 2H), 5.80 (s, 1H), 2.96 (ddd, J = 13.7, 7.1, 4.0 Hz, 1H), 2.63 (ddd, J = 15.8, 11.2, 7.1 Hz, 1H), 2.48 (dd, J = 13.7, 2.6 Hz, 1H), 2.43 (s, 1H), 2.35 (ddd, J = 15.8, 6.5, 4.0 Hz, 1H), 2.14 (dq, J = 13.3, 3.7, 3.0 Hz, 1H), 2.06 (td, J = 13.7, 4.3 Hz, 1H), 1.89 (td, J = 13.7, 4.6 Hz, 1H), 1.79 (t, J = 13.7 Hz, 1H), 1.73 – 1.53 (m, 4H), 1.52 – 1.45 (m, 1H), 1.44 (s, 3H), 1.43 – 1.39 (m, 1H), 1.39 (s, 3H), 1.30 (dd, J = 10.9, 3.5 Hz, 1H), 1.26 (s, 3H), 1.22 (m, 1H), 1.18 (s, 3H), 1.10 (s, 3H), 1.08 (m, 1H), 1.06 (s, 3H), 0.92 (s, 3H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 217.39, 199.48, 172.73, 169.04, 162.23, 134.88, 129.15, 128.90, 124.07, 61.20, 55.57, 47.92, 47.88, 45.32, 44.03, 43.36, 41.42, 39.88, 37.37, 36.85, 34.38, 32.26, 31.99, 31.54, 28.52, 28.08, 26.68, 26.57, 26.53, 23.44, 21.57, 18.93, 18.67, 15.81.

HRMS: (ESI-TOF) calculated for C₃₈H₄₈NO₆⁺ ([M+H]⁺): 614.34761, found 614.3478.

FTIR (thin film, cm⁻¹): ν 3305 (w), 2964 (w), 2947 (w), 2873 (w), 2848 (w), 2360 (w), 2340 (w), 2185 (w), 2050 (w), 2026 (w), 1978 (w), 1726 (s), 1681 (m), 1643 (s), 1617 (w), 1444 (w), 1385 (m), 1362 (w), 1347 (w), 1328 (w), 1279 (w), 1250 (w), 1205 (m), 1193 (w), 1175 (w), 1142 (m), 1110 (w), 1086 (m), 1071 (w), 1049 (w), 1028 (w), 989 (w), 982 (w), 948 (w), 885 (w), 873 (w), 822 (w), 779 (m), 747 (w), 727 (w), 692 (w), 669 (m), 622 (w), 605 (w), 584 (m), 560 (w), 537 (w), 479 (w), 461 (w), 418 (w), 403 (w).

1,3-dioxoisindolin-2-yl 2-(4-(tert-butyl)phenoxy)acetate (S26)

Synthesized according to general procedure A with 2-(4-(tert-butyl)phenoxy)acetic acid (0.8435 g, 4.0 mmol, 1 equiv.), *N*-hydroxyphthalimide (0.9814 g, 6.0 mmol, 1.5 equiv.), DMAP (35.0 mg, 0.2 mmol, 0.05 equiv.) and DIC

(0.9 mL, 5.4 mmol, 1.4 equiv.). Purified over silica with flash chromatography (5 to 25% EtOAc in hexanes) to afford the title compound as a white solid (1.0869 g, 3.08 mmol, 76%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.91 (dd, J = 5.4, 3.1 Hz, 2H), 7.81 (dd, J = 5.5, 3.1 Hz, 2H), 7.35 (d, J = 8.9 Hz, 2H), 6.93 (d, J = 8.9 Hz, 2H), 5.02 (s, 2H), 1.30 (s, 9H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 165.88, 161.69, 155.24, 145.33, 135.08, 128.93, 126.69, 124.28, 114.46, 63.73, 34.33, 31.60.

HRMS: (ESI-TOF) calculated for C₂₀H₁₉NNaO₅⁺ ([M+Na]⁺): 376.11554, found 376.11562.

FTIR (thin film, cm⁻¹): ν 2946 (w), 2858 (w), 1844 (m), 1795 (m), 1737 (s), 1607 (m), 1582 (w), 1511 (s), 1479 (w), 1467 (m), 1434 (m), 1411 (w), 1392 (w), 1364 (m), 1298 (m), 1245 (s), 1187 (m), 1159 (w), 1138 (m), 1118 (m), 1103 (m), 1067 (s), 1014 (m), 967 (s), 913 (s), 875 (s), 848 (m), 824 (s), 804 (m), 787 (s), 727 (w), 696 (s), 669 (m), 602 (m), 575 (m), 550 (s), 518 (s), 472 (m), 443 (w).

1,3-dioxoisindolin-2-yl 2-((4-bromophenyl)thio)acetate (S27)

According to literature procedure,⁸ to a 100 mL flask with a stir bar was added 4-bromothiophenol (1.9917 g, 10.5 mmol, 1 equiv.), sodium hydroxide (1.63 g, 40.8 mmol, 4 equiv.), and 2-bromoacetic acid (2.04 g, 14.68 mmol, 1.4 equiv.). The flask was then charged with 30 mL of water and allowed to stir overnight at room temperature. The reaction mixture was acidified using 1 N HCl. The reaction mixture was decanted to a separatory funnel and extracted 3 times with ether. The combined ethereal extracts were dried, filtered, and concentrated to produce a slightly yellow solid residue. Purified over silica with flash chromatography (25 to 100% EtOAc in hexanes) to afford the title compound as a white solid (2.2446 g, 9.08 mmol, 94%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.44 (d, J = 8.5 Hz, 2H), 7.29 (d, J = 8.6 Hz, 2H), 3.65 (s, 2H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 175.14, 133.58, 132.30, 131.73, 121.49, 36.49.

Synthesized according to general procedure A with the acid from the previous step (0.9851 g, 4 mmol, 1 equiv), N-hydroxyphthalimide (0.9947 g, 6 mmol, 1.5 equiv), DMAP (34.2 mg, 0.2 mmol, 0.05 equiv) and DIC (0.9 mL, 5.4 mmol, 1.4 equiv). Purified over silica with flash chromatography (5 to 25% EtOAc in hexanes) to afford the title compound as a white solid (1.2215 g, 3.11 mmol, 78%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.89 (dd, J = 5.4, 3.1 Hz, 2H), 7.80 (dd, J = 5.5, 3.1 Hz, 2H), 7.49 (d, J = 8.7 Hz, 2H), 7.45 (d, J = 8.6 Hz, 2H), 3.86 (s, 2H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 166.20, 161.71, 135.05, 133.80, 132.61, 132.37, 128.93, 124.24, 122.88, 34.66.

HRMS: (ESI-TOF) calculated for C₁₆H₁₁BrNO₄S⁺ ([M+H]⁺): 391.95867, found 391.95748.

FTIR (thin film, cm⁻¹): ν 3095 (w), 2938 (w), 1818 (m), 1789 (m), 1739 (s), 1609 (w), 1475 (m), 1466 (m), 1365 (m), 1352 (m), 1325 (m), 1282 (m), 1185 (m), 1118 (m), 1092 (m), 1059 (s), 1015 (m), 1002 (s), 964 (s), 867 (s), 808 (s), 781 (s), 725 (m), 692 (s), 601 (s), 550 (m), 518 (s), 489 (s), 475 (s), 408 (m).

**1,3-dioxoisindolin-2-yl
carboxylate (S28)****(3*aS*,4*S*,6*R*,6*aR*)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxole-4-**

According to literature method,⁹ to a 100- mL flask with a stir bar was added D-ribose (3.0115 g, 20 mmol, 1 equiv.), benzyl alcohol (20 mL, 190 mmol, 10 equiv.), and 12.0 mL of acetone. Sulfuric acid (6 drops) was added and the reaction mixture was heated to 75 °C for 5 hours. The reaction was cooled to room temperature and then neutralized by the addition of triethylamine until basic. Volatiles were removed via rotary evaporation. The resulting yellow solution was washed with water, dried over sodium sulfate, filtered, and concentrated. The resulting solution was concentrated via vacuum distillation to remove as much benzyl alcohol as possible. Upon cooling, a brown solid precipitated. Purified over silica with flash chromatography (5 to 40% EtOAc in hexanes) to yield ((3*aR*,4*R*,6*R*,6*aR*)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)methanol as a white solid (1.4447 g, 26% yield).

Note: Washing and/or sonication of the white solid with hexanes was important to remove all benzyl alcohol prior to subsequent oxidation to the carboxylic acid.

¹H NMR (500 MHz, Chloroform-*d*): δ 7.39 – 7.30 (m, 5H), 5.18 (s, 1H), 4.86 (d, *J* = 5.9 Hz, 1H), 4.77 (d, *J* = 11.6 Hz, 1H), 4.67 (d, *J* = 5.9 Hz, 1H), 4.58 (d, *J* = 11.6 Hz, 1H), 4.46 (t, *J* = 3.0 Hz, 1H), 3.72 (dd, *J* = 12.6, 2.3 Hz, 1H), 3.64 (dt, *J* = 11.6, 5.9 Hz, 1H), 3.13 (d, *J* = 10.2 Hz, 1H), 1.48 (s, 3H), 1.32 (s, 3H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 136.46, 128.83, 128.43, 128.37, 112.28, 108.19, 88.63, 86.15, 81.65, 70.35, 64.22, 26.48, 24.80.

According to literature conditions,¹⁰ to a 100-mL flask equipped with a stir bar was ((3*aR*,4*R*,6*R*,6*aR*)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)methanol (1.4016 g, 5 mmol, 1 equiv), sodium chlorite (1.3820 g, 15 mmol, 3 equiv), and TEMPO (62.1 mg, 0.4 mmol, 0.08 equiv). The flask was charged with 20 mL of phosphate buffer (6.7 M, 6.8 pH sodium phosphate buffer) and 25 mL of MeCN. The reaction mixture was heated to 35 °C and stirred. Sodium hypochlorite (0.4 mL of a 12% solution) was added dropwise over 2 hours. The reaction mixture was stirred overnight at 35 °C. The reaction mixture was poured into a 10% sodium hydroxide solution and extracted with ether. The organics were separated and discarded. The aqueous layer was carefully acidified using 1 N HCl to pH 4. The reaction mixture was then extracted 3 times with ether. The combined organics were separated, dried over sodium sulfate, filtered, and then concentrated to produce a yellow oil. Purified over silica with flash chromatography to afford (3*aS*,4*S*,6*R*,6*aR*)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxole-4-carboxylic acid as a clear oil that solidified to a white solid upon standing (0.7245 g, 2.46 mmol, 49%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.40 – 7.30 (m, 5H), 5.29 (d, *J* = 1.8 Hz, 1H), 5.23 (d, *J* = 5.9 Hz, 1H), 4.87 (dd, *J* = 11.7, 1.7 Hz, 1H), 4.73 (s, 1H), 4.68 (dd, *J* = 5.9, 1.8 Hz, 1H), 4.59 (dd, *J* = 11.6, 1.7 Hz, 1H), 1.51 (s, 3H), 1.35 (s, 3H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 173.67, 136.68, 128.70, 128.25, 128.20, 113.12, 107.64, 84.50, 83.99, 82.34, 70.10, 26.44, 25.02.

Synthesized according to general procedure A with the acid from the previous step (0.7245 g, 2.46 mmol, 1 equiv.), *N*-hydroxyphthalimide (0.6002 g, 3.8 mmol, 1.5 equiv.), DMAP (25.7 mg, 0.21 mmol, 0.085 equiv.) and DIC (0.6 mL, 1.87 mmol, 1.6 equiv). Purified over silica with flash chromatography (10 to 25% EtOAc in hexanes) to afford the title compound as a sticky white solid (0.8261 g, 1.88 mmol, 76%).

¹H NMR (400 MHz, Chloroform-*d*): δ 7.90 (dd, J = 5.5, 3.1 Hz, 2H), 7.80 (dd, J = 5.5, 3.1 Hz, 2H), 7.36 – 7.26 (m, 5H), 5.41 (dd, J = 5.8, 1.3 Hz, 1H), 5.28 (s, 1H), 5.07 – 5.06 (m, 1H), 4.96 (d, J = 12.4 Hz, 1H), 4.75 – 4.72 (m, 1H), 4.60 (d, J = 12.4 Hz, 1H), 1.51 (s, 3H), 1.35 (s, 3H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 166.92, 161.62, 137.03, 135.01, 129.02, 128.59, 128.57, 127.99, 124.22, 113.46, 106.81, 84.55, 82.65, 82.62, 69.57, 26.56, 25.18.

HRMS: (ESI-TOF) calculated for C₂₃H₂₂NO₈⁺ ([M+H]⁺): 440.13399, found 440.13329.

FTIR (thin film, cm⁻¹): ν 2354 (m), 2340 (w), 2057 (w), 2047 (w), 2030 (w), 2017 (w), 2009 (w), 1992 (w), 1968 (w), 1813 (w), 1790 (w), 1741 (s), 1700 (w), 1685 (w), 1653 (w), 1636 (w), 1466 (w), 1457 (w), 1373 (w), 1210 (w), 1186 (w), 1158 (w), 1132 (w), 1078 (m), 1042 (m), 965 (m), 938 (m), 904 (m), 875 (m), 862 (m), 783 (w), 738 (m), 693 (s), 603 (w), 516 (m), 457 (w), 436 (w), 419 (w), 407 (w).

1,3-dioxoisindolin-2-yl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate (S29)

Prepared according to general procedure B with fenofibric acid (2-[4-(4-Chlorobenzoyl)phenoxy]-2-methylpropionic acid, 1.2509 g, 3.92 mmol, 1 equiv.), DMF (5 drops, catalytic), and oxalyl chloride (0.6 mL, 7.1 mmol, 1.75 equiv.) followed by *N*-hydroxyphthalimide (0.6795 g, 4.17 mmol, 1.06 equiv.) and triethylamine (0.6 mL, 4.30 mmol, 1.1 equiv.). Purified via column chromatography (15-25% EtOAc/hexanes). This afforded the title compound as a white solid (1.4510 g, 3.13 mmol, 80%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.90 (dd, J = 5.5, 3.1 Hz, 2H), 7.86 – 7.79 (m, 4H), 7.74 (d, J = 8.5 Hz, 2H), 7.46 (d, J = 8.6 Hz, 2H), 7.12 (d, J = 8.8 Hz, 2H), 1.88 (s, 6H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 194.45, 170.50, 161.86, 158.71, 138.62, 136.44, 135.10, 132.24, 131.60, 131.41, 129.01, 128.73, 124.25, 118.65, 78.77, 25.87.

HRMS: (ESI-TOF) calculated for C₂₅H₁₉ClNO₆⁺ ([M+H]⁺): 464.08954, found 464.08910.

FTIR (thin film, cm⁻¹): ν 3017.57 (w), 1840.21 (w), 1811.43 (m), 1784.61 (s), 1744.45 (s), 1659.00 (s), 1597.77 (s), 1588.11 (s), 1501.55 (m), 1486.74 (m), 1467.20 (m), 1455.57 (m), 1398.41 (m), 1388.08 (m), 1352.14 (m), 1317.38 (s), 1299.68 (s), 1286.12 (m), 1272.64 (s), 1234.47 (s), 1202.19 (m), 1184.23 (s), 1169.78 (s), 1147.78 (s), 1128.67 (s), 1088.98 (s), 1080.00 (s), 1046.00 (s), 1013.51 (s), 961.51 (s), 928.90 (s), 907.65 (s), 876.72 (s), 854.82 (s), 830.17 (s), 783.67 (s), 761.21 (s), 748.91 (s), 738.14 (m), 722.95 (m), 709.20 (s), 692.92 (s), 675.74 (s).

1,3-dioxoisindolin-2-yl 2-(4-(4-cyano-2-fluorophenoxy)phenoxy)propanoate (S30)

To a 100-mL flask with a stir bar was added cyhalofop butyl (butyl (*R*)-2-[4-(4-cyano-2-fluorophenoxy)phenoxy]propionate, 1.027 g, 2.8 mmol, 1 equiv.) and 14 mL methanol (0.2 M). Then 1.5 mL 6 M NaOH (3.2 equiv.) was added in one portion and the reaction was stirred at room temperature overnight. The reaction mixture was then concentrated and extracted with 20 mL of ether three times. The aqueous layer was then acidified to pH 1 and extracted with 30 mL DCM three times. The organic layers were washed with water, brine and dried over Na₂SO₄ and concentrated to yield a cloudy-white solid. The solid was then purified by column chromatography with 10% - 20% MeOH:DCM to afford quantitative yield of ().

¹H NMR (500 MHz, Chloroform-*d*): δ 7.46 (dd, J = 10.1, 2.0 Hz, 1H), 7.35 (dt, J = 8.5, 1.7 Hz, 1H), 7.02 (d, J = 9.1 Hz, 2H), 6.94 (d, J = 9.1 Hz, 2H), 6.89 (t, J = 8.3 Hz, 1H), 4.80 (q, J = 6.8 Hz, 1H), 1.69 (d, J = 6.8 Hz, 3H).

¹⁹F NMR (282 MHz, Chloroform-*d*): δ -129.84 (t, J = 9.3 Hz).

Synthesized according to general procedure A with the acid from the previous step (1.00 g, 3.32 mmol, 1 equiv.), *N*-hydroxyphthalimide (0.7356 g, 4.5 mmol, 1.36 equiv), DMAP (18.6 mg, 0.15 mmol, 0.048 equiv) and DIC (0.66 mL, 4.26 mmol, 1.28 equiv.). The reaction mixture turned golden orange over the reaction period (72 hrs). Purified over silica with flash chromatography (10 to 30% EtOAc in hexanes) to afford the title compound as a white solid (0.6535 g, 1.46 mmol 49%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.89 (dd, J = 5.5, 3.1 Hz, 2H), 7.81 (dd, J = 5.5, 3.0 Hz, 2H), 7.46 (dd, J = 10.1, 2.0 Hz, 1H), 7.35 (dt, J = 8.6, 1.6 Hz, 1H), 7.06 (d, J = 1.7 Hz, 4H), 6.91 (t, J = 8.3 Hz, 1H), 5.09 (q, J = 6.8 Hz, 1H), 1.89 (d, J = 6.8 Hz, 3H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 168.64, 161.69, 154.53, 152.51 (d, J = 252.0 Hz), 150.59 (d, J = 10.6 Hz), 149.32, 135.13, 129.55 (d, J = 3.9 Hz), 128.91, 124.27, 121.41, 120.70 (d, J = 21.2 Hz), 118.84, 117.87 (d, J = 2.6 Hz), 117.20, 106.19 (d, J = 8.1 Hz), 71.77, 19.08.

¹⁹F NMR (282 MHz, CDCl₃): δ -130.00 (t, J = 9.4 Hz).

HRMS: (ESI-TOF) calculated for C₂₄H₁₅FN₂NaO₆⁺ ([M+Na]⁺): 469.08064, found 469.0803.

FTIR (thin film, cm⁻¹): ν 2232 (w), 1819 (w), 1788 (m), 1740 (s), 1614 (w), 1584 (w), 1496 (s), 1467 (m), 1424 (w), 1358 (w), 1282 (s), 1243 (m), 1218 (s), 1185 (s), 1114 (s), 1069 (s), 1037 (s), 962 (s), 945 (s), 875 (s), 841 (s), 803 (m), 785 (s), 693 (s), 611 (s), 565 (m), 535 (m), 517 (s), 460 (m), 409 (m).

1,3-dioxoisindolin-2-yl 2-([1,1'-biphenyl]-4-yl)-2-fluoroacetate (S31)

2-([1,1'-biphenyl]-4-yl)-2-fluoroacetic acid was prepared according to the procedure from Gouverneur.¹¹ To an oven-dried 100-mL flask equipped with a stir bar was added 4-biphenylacetic acid (2.1984 g, 10.36 mmol, 1 equiv.) and 3.77 g TBSCl (3.77 g, 25 mmol, 2.4 equiv.). The flask was septa capped and put under vacuum and refilled with nitrogen three times. THF (10 mL, anhydrous) was added to the flask and the solution was stirred at 0°C. Then, LiHMDS (22 mL, 1M solution in THF, 22 mmol) was added dropwise over 20 minutes and the reaction mixture turned from cloudy yellow to a clear brown solution overnight. The resulting solution was concentrated *in vacuo* and the crude bis-silylketenacetal was dissolved in hexanes (50 mL) and the LiCl was filtered off. The solid was washed with an additional 50 mL hexane and the filtrate was concentrated *in vacuo*. The residue was redissolved in 20 mL acetonitrile and added dropwise to a solution of Selectfluor® (4.8 g, 13.5 mmol, 1.3 equiv.) in acetonitrile (40 mL) at room temperature. The solution was stirred at room temperature overnight. The reaction was then poured into 100 mL 1 M HCl and extracted with 100 mL Et₂O twice. The combined ether layers were extracted with 60 mL 1M NaOH twice and the combined basic layers were washed with 200 mL Et₂O twice. The basic aqueous layer was acidified to pH 1 with 6 M HCl, then extracted with 200 mL Et₂O twice. The combined ether layers were dried over Na₂SO₄ and concentrated under reduced pressure. The crude residue was used directly for phthalimide ester synthesis.

Prepared according to general procedure A, using the crude residue from above, *N*-hydroxyphthalimide (2.44 g, 15.0 mmol, 1.4 equiv.), DMAP (68.2 mg, 0.56 mmol, 0.05 equiv.), and DIC (2.0 mL, 12.9 mol, 1.25 equiv.). The reaction started turned an orange that faded to a pale yellow as the reaction proceeded. The residue was purified by (10 to 30% EtOAc in hexanes). This afforded 1.256 g of 1,3-dioxoisindolin-2-yl 2-([1,1'-biphenyl]-4-yl)-2-fluoroacetate as an off-yellow solid with some trace impurities. 1.055 g of the compound was recrystallized from 80 mL Et₂O at 50°C

and left in a freezer for 24 hours. The mother liquor was removed and the solid was washed with cold ether and dried to yield the title compound as an off-white solid (663.5 mg, 1.77 mmol, 18% overall yield).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.90 (dd, J = 5.5, 3.1 Hz, 2H), 7.81 (dd, J = 5.5, 3.1 Hz, 2H), 7.73 (d, J = 8.3 Hz, 2H), 7.69 (dd, J = 8.3, 1.6 Hz, 2H), 7.62 (dd, J = 8.3, 1.3 Hz, 2H), 7.47 (t, J = 7.7 Hz, 2H), 7.42 – 7.36 (m, 1H), 6.24 (d, J = 47.2 Hz, 1H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 165.29 (d, J = 29.5 Hz), 161.41, 143.75 (d, J = 2.9 Hz), 140.22, 135.15, 131.19 (d, J = 19.9 Hz), 129.04, 128.88, 128.27 (d, J = 5.0 Hz), 128.04, 128.03, 127.41, 124.32, 88.17 (d, J = 189.2 Hz).

¹⁹F NMR (282 MHz, Chloroform-*d*): δ -179.17 (d, J = 47.6 Hz).

HRMS: (ESI-TOF) calculated for C₂₂H₁₄FNNaO₄⁺ ([M+Na]⁺): 398.07991, found 398.0797.

FTIR (thin film, cm⁻¹): ν 3102 (w), 3045 (w), 2361 (m), 2339 (m), 1819 (w), 1791 (w), 1742 (m), 1610 (w), 1487 (m), 1464 (s), 1409 (m), 1358 (m), 1294 (m), 1185 (m), 1171 (m), 1112 (m), 1080 (w), 1047 (m), 1007 (w), 960 (m), 931 (w), 873 (m), 839 (w), 792 (m), 754 (w), 695 (w), 668 (w), 624 (w), 594 (m), 551 (m), 528 (m), 517 (w), 491 (w), 436 (w), 408 (w).

1,3-dioxoisindolin-2-yl 3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (S32)

Prepared according to general procedure B, using Mosher's acid (3,3,3-trifluoro-2-methoxy-2-phenylpropanoic acid, 0.9667 g, 4.13 mmol, 1 equiv.), DMF (5 drops), and oxalyl chloride (0.6 mL, 7.09 mmol, 1.72 equivalent), followed by *N*-hydroxyphthalimide (0.7429 g, 4.55 mmol, 1.10 equiv.) and triethylamine (0.6 mL, 4.30 mmol, 1.04 equiv.) Purified by column chromatography (10-25% EtOAc in hexanes). This afforded the title compound as a white solid (1.1070 g, 71%, 2.92 mmol).

¹H NMR (500 MHz, Chloroform-*d*): 7.92 (dd, J = 5.5, 3.1 Hz, 2H), 7.83 (dd, J = 5.5, 3.1 Hz, 2H), 7.75 – 7.68 (m, 2H), 7.53 – 7.46 (m, 3H), 3.82 (q, J = 1.4 Hz, 3H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 163.96, 161.43, 135.22, 131.01, 130.43, 128.90, 128.74, 127.57, 124.35, 122.80 (q, J = 289.0 Hz), 85.02 (q, J = 28.9 Hz), 56.66 (q, J = 1.5 Hz).

¹⁹F NMR (282 MHz, Chloroform-*d*): δ -72.31 (s, 3F).

HRMS: (ESI-TOF) calculated for C₁₈H₁₂FNNaO₅⁺ ([M+Na]⁺): 402.05598, found 402.05513.

FTIR (thin film, cm⁻¹): ν 408.3 (m), 516.2 (s), 592.1 (m), 640.9 (m), 692.2 (s), 729.8 (s), 764.7 (s), 788.8 (m), 838.1 (m), 873.4 (s), 900.7 (m), 926.1 (m), 981.8 (s), 1000.8 (m), 1016.3 (m), 1036.0 (m), 1079.2 (s), 1117.2 (s), 1155.6 (s), 1167.5 (s), 1184.0 (s), 1228.5 (m), 1267.6 (m), 1289.8 (m), 1324.3 (w), 1353.2 (m), 1452.4 (m), 1469.3 (m), 1495.4 (w), 1608.5 (w), 1738.4 (s), 1789.3 (m), 1815.2 (m), 2850.3 (w), 2956.8 (w).

1,3-dioxoisindolin-2-yl 9-fluoro-9H-fluorene-9-carboxylate (S33)

9-fluorene-9-carboxylic acid was prepared according to the procedure from Gouverneur.¹¹ To an oven-dried 100-mL flask with a stir bar was added fluorene-9-carboxylic acid (2.1628 g, 10.3 mmol, 1 equiv.) and 3.487 g TBSCl (3.487 g, 23.1 mmol). The flask was septa capped and put under vacuum and refilled with nitrogen three times. 10 mL of anhydrous THF was added to the flask and the solution was stirred at 0°C. Then, 22 mL of LiHMDS (1M solution in THF, 22 mmol) was added dropwise over 20 minutes and the reaction mixture turned from cloudy yellow to a clear brown solution overnight. The resulting solution was concentrated in vacuo and the crude bis-silylketenacetal

was dissolved in 50 mL hexane and the LiCl was filtered off. The solid was washed with 50 mL hexane and the filtrate was concentrated under reduced pressure. The residue was dissolved in 20 mL acetonitrile and added dropwise to a solution of Selectfluor (4.6 g, 13 mmol) in acetonitrile (40 mL) at room temperature. The solution was stirred at room temperature overnight. The reaction was then poured into 100 mL 1 M HCl and extracted with 100 mL Et₂O twice. The combined ether layers were extracted with 60 mL 1M NaOH twice and the combined basic layers were washed with 200 mL Et₂O twice. The basic aqueous layer was acidified to pH 1 with 6 M HCl, then extracted with 200 mL Et₂O twice. The combined ether layers were dried over Na₂SO₄ and concentrated under reduced pressure. The crude residue was used directly for phthalimide ester synthesis.

Prepared according to general procedure A, using the crude residue from above, *N*-hydroxyphthalimide (1.64 g, 10.1 mmol, 0.98 equiv.), DMAP (66.8 mg, 0.55 mmol, 0.05 equiv.), and DIC (2.2 mL, 15.2 mmol, 1.4 equiv.). The reaction started turned an orange that faded to a pale yellow as the reaction proceeded. The residue was purified by (10 to 30% EtOAc in hexanes). This afforded 1,3-dioxoisindolin-2-yl 9-fluoro-9H-fluorene-9-carboxylate as an off-yellow solid with some trace impurities. The compound was recrystallized from 60 mL Et₂O and 5 mL DCM at 45°C and left in a freezer for 24 hours. Then, 7 mL hexane was added to the solution to crash out any remaining phthalimide ester. The mother liquor was removed and the solid was washed with cold ether and dried to yield the title compound as a light-yellow solid (660.7 mg, 1.77 mmol, 18%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.84 (dd, J = 5.5, 3.1 Hz, 2H), 7.79 – 7.74 (m, 4H), 7.68 (d, J = 7.5 Hz, 2H), 7.53 (td, J = 7.6, 1.4 Hz, 2H), 7.42 (t, J = 7.6 Hz, 2H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 166.55 (d, J = 36.2 Hz), 161.31, 141.43 (d, J = 2.4 Hz), 139.24 (d, J = 18.7 Hz), 135.03, 131.99 (d, J = 2.1 Hz), 129.05 (d, J = 1.9 Hz), 128.87, 125.59, 124.17, 120.91, 97.07 (d, J = 197.0 Hz).

¹⁹F NMR (282 MHz, CDCl₃): δ -160.39 (s, 1F).

HRMS: (ES-TOF) calculated for C₂₂H₁₂FN₂O₄⁺ ([M⁺]): 373.07449, found 373.07426.

FTIR (thin film, cm⁻¹): ν 3339 (w), 3052 (w), 2967 (w), 1817 (s), 1788 (s), 1746 (s), 1653 (w), 1608 (m), 1572 (m), 1488 (w), 1466 (m), 1451 (s), 1419 (w), 1360 (m), 1325 (m), 1292 (w), 1233 (m), 1205 (m), 1187 (m), 1160 (s), 1128 (s), 1106 (m), 1079 (m), 1034 (s), 973 (s), 950 (s), 938 (s), 930 (s), 873 (s), 829 (m), 781 (m), 764 (s), 748 (s), 726 (s), 708 (s), 688 (s), 619 (s), 595 (s), 575 (s), 515 (s), 427 (s), 416 (s).

1,3-dioxoisindolin-2-yl (2-phenylpropan-2-yl) oxalate (S34)

The phthalimidoyl oxalate was prepared according to literature precedent from Overman.¹² To an oven-dried 100-mL flask equipped with a stir bar with was added 2-phenyl-2-propanol (430 μ L, 3.07 mmol, 1 equiv.), DMAP (43.1 mg, 0.35 mmol, 0.11 equiv.), and triethylamine (0.85 mL, 6.10 mmol, 2.0 equiv.). Then 50 mL of a 0.06 M solution of chloro-*N*-phthalimidoyl oxalate in THF (3.0 mmol, 0.98 equiv.) was added dropwise. The resulting mixture was stirred overnight at room temperature. The volatiles were removed under reduced pressure and the crude mixture was dissolved in 25 mL dichloromethane and transferred to an Erlenmeyer flask containing 400 mL hexanes. Brown solid crashed out immediately and the solution was filtered over a frit and washed with hexanes (4 x 25 mL). The filtrate was concentrated to yield the title compound as an off yellow-white solid (0.9612 g, 2.72 mmol, 89%, 62% molar purity contaminated with 2-phenyl-2-propanol).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.93 (dd, J = 5.5, 3.1 Hz, 2H), 7.83 (dd, J = 5.5, 3.1 Hz, 2H), 7.47 (dd, J = 8.4, 1.3 Hz, 2H), 7.41 – 7.37 (m, 2H), 7.30-7.34 (m, 1H), 1.96 (s, 6H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 161.06, 154.33, 152.78, 143.41, 135.21, 128.87, 128.78, 128.08, 124.64, 124.42, 88.26, 28.25.

FTIR (thin film, cm⁻¹): ν 2956 (w), 2850 (w), 1815 (m), 1789 (m), 1738 (s), 1609 (w), 1495 (w), 1469 (m), 1452 (m), 1353 (m), 1324 (w), 1290 (m), 1268 (m), 1229 (m), 1184 (s), 1168 (s), 1156 (s), 1117 (s), 1079 (s), 1036 (m), 1016 (m), 1001 (m), 982 (s), 926 (m), 901 (m), 873 (s), 838 (m), 789 (m), 765 (s), 730 (s), 692 (s), 641 (m), 592 (m), 516 (s), 408 (m).

This phthalimidoyl oxalate proved too unstable to obtain HRMS data via ESI.

1,3-dioxoisindolin-2-yl (2-methyl-4-phenylbutan-2-yl) oxalate (S35)

The phthalimidoyl oxalate was prepared according to literature precedent from Overman.¹² To an oven-dried 100-mL flask with a stir bar was added 2-methyl-4-phenyl-2-butanol (1.00 mL, 5.88 mmol, 1 equiv.), DMAP (80.5 mg, 0.66 mmol, 0.11 equiv.), and triethylamine (1.7 mL, 12.2 mmol, 2.1 equiv.). Then 200 mL of a 0.06 M solution of chloro-*N*-phthalimidoyl oxalate in THF was added dropwise (12 mmol, 2.0 equiv.). The resulting mixture was stirred overnight at room temperature. The volatiles were removed under reduced pressure and the crude mixture was dissolved in 60 mL dichloromethane and transferred to an Erlenmeyer flask containing 600 mL hexanes. A brown precipitate formed immediately and the suspension was filtered through frit. The filtered solids were washed with hexanes (4 x 50 mL). The filtrate was concentrated to yield the title compound as a brown-yellow oil (2.13 g, 5.58 mmol, 95%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.93 (dd, J = 5.5, 3.1 Hz, 1H), 7.83 (dd, J = 5.5, 3.1 Hz, 1H), 7.31 – 7.27 (m, 2H), 7.23 – 7.17 (m, 3H), 2.77 – 2.72 (m, 2H), 2.21 – 2.17 (m, 2H), 1.69 (s, 6H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 161.07, 154.45, 153.16, 141.36, 135.19, 128.85, 128.64, 128.48, 126.19, 124.39, 89.41, 42.84, 30.34, 25.74.

FTIR (thin film, cm⁻¹): ν 2957 (w), 2850 (w), 1815 (m), 1789 (m), 1738 (s), 1609 (w), 1495 (w), 1469 (m), 1452 (m), 1353 (m), 1324 (w), 1290 (m), 1268 (m), 1229 (m), 1184 (s), 1168 (s), 1156 (s), 1117 (s), 1079 (s), 1036 (m), 1016 (m), 1001 (m), 982 (s), 926 (m), 901 (m), 873 (s), 838 (m), 789 (m), 765 (s), 730 (s), 692 (s), 641 (m), 592 (m), 516 (s), 408 (m).

This phthalimidoyl oxalate proved too unstable to obtain HRMS data via ESI.

V. Isolation and characterization of product compounds

2-(1-fluoroethyl)-6-methoxynaphthalene (2)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 2-(6-methoxynaphthalen-2-yl)propanoate (0.2276 g, 0.606 mmol, 1 equiv.), Ir(dF-ppy)₃ (3.8 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M). Purified over silica with flash chromatography (10% ether in pentanes) to afford the title compound as a white solid (111.3 mg, 0.545 mmol, 90%). A second run with 1,3-dioxoisindolin-2-yl 2-(6-methoxynaphthalen-2-yl)propanoate (0.2255 g, 0.601 mmol, 1 equiv.), Ir(dF-ppy)₃ (3.6 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3 mL, 0.2 M) afforded 110.0 mg (90%, 0.539 mmol).

Scale up protocol:

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 2-(6-methoxynaphthalen-2-yl)propanoate (1.481 g, 3.95 mol, 1 equiv.), Ir(dF-ppy)₃ (30.6 mg, 0.04 mmol, 0.01 equiv.), triethylamine trihydrofluoride (978 μ L, 6.0 mmol, 1.5 equiv.), and DCM (10.00 mL, 0.4 M). Purified over silica with flash chromatography (3% ether in hexanes) to afford the title compound as a white solid (600.2 mg, 2.94 mmol, 75%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.77 – 7.72 (m, 3H), 7.45 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.17 (dd, *J* = 8.8, 2.5 Hz, 1H), 7.14 (d, *J* = 2.5 Hz, 1H), 5.76 (dq, *J* = 47.6, 6.4 Hz, 1H), 3.93 (s, 3H), 1.73 (dd, *J* = 23.7, 6.4 Hz, 3H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 158.08, 136.61 (d, *J* = 19.4 Hz), 134.55 (d, *J* = 1.6 Hz), 129.72, 128.64, 127.34, 124.40 (d, *J* = 7.7 Hz), 123.94 (d, *J* = 5.4 Hz), 119.31, 105.79, 91.38 (d, *J* = 166.9 Hz), 55.47, 22.99 (d, *J* = 25.5 Hz).

¹⁹F NMR (376 MHz, Chloroform-*d*): -164.98 (dq, *J* = 47.6, 23.6 Hz).

HRMS: (EI-TOF) calculated for C₁₃H₁₃FO⁺ [*M*⁺]: 204.09449, found 204.09542.

FTIR (thin film, cm⁻¹): ν 2962 (w), 2933 (w), 1633 (m), 1605 (s), 1505 (m), 1486 (s), 1462 (m), 1391 (m), 1374 (m), 1353 (m), 1314 (m), 1266 (m), 1237 (m), 1218 (m), 1196 (m), 1177 (s), 1162 (s), 1063 (m), 1028 (s), 993 (m), 961 (m), 929 (m), 900 (m), 870 (m), 853 (s), 816 (s), 751 (m), 672 (m).

1-(*tert*-butyl)-4-(fluoromethyl)benzene (7)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 2-(4-(*tert*-butyl)phenyl)acetate (0.2730 g, 0.809 mmol, 1 equiv.), Ir(dF-ppy)₃ (4.2 mg, 0.008 mmol, 0.01 equiv.), triethylamine trihydrofluoride (391.2 μ L, 2.4 mmol, 3 equiv.), and DCM (4.00 mL, 0.2 M). Purified by preparatory TLC (10% ether in pentanes) to afford the title compound as a slightly yellow oil (89.8 mg, 0.540 mmol, 67%). A second run with 1,3-dioxoisindolin-2-yl 2-(4-(*tert*-butyl)phenyl)acetate (277.5 mg, 0.823 mmol, 1 equiv.), Ir(dF-ppy)₃ (4.2 mg, 0.008 mmol, 0.01 equiv.), triethylamine trihydrofluoride (391.2 μ L, 2.4 mmol, 3 equiv.), and DCM (4.00 mL, 0.2 M) afforded 83.5 mg (0.502 mmol, 61%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.43 (dd, *J* = 8.2, 1.7 Hz, 2H), 7.34 (dd, *J* = 8.3, 2.0 Hz, 2H), 5.36 (d, *J* = 47.5 Hz, 2H), 1.34 (s, 9H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 152.10 (d, *J* = 3.4 Hz), 133.34 (d, *J* = 17.1 Hz), 127.77 (d, *J* = 5.4 Hz), 125.70, 84.71 (d, *J* = 164.9 Hz), 34.81, 31.44.

¹⁹F NMR (282 MHz, Chloroform-*d*): δ -204.37 (t, *J* = 48.1 Hz).

HRMS: (EI-TOF) calculated for C₁₁H₁₅F⁺ [*M*⁺]: 166.11523, found: 166.11604

FTIR (thin film, cm⁻¹): ν 2961 (s), 2902 (m), 2869 (m), 1616 (w), 1514 (w), 1465 (m), 1411 (w), 1394 (w), 1364 (s), 1269 (m), 1223 (m), 1203 (w), 1108 (m), 980 (s), 851 (m), 833 (s), 810 (s), 741 (w), 671 (m), 572 (m), 524 (m), 453 (w), 429 (w), 418 (w), 405 (w).

4-(fluoromethyl)-1,1'-biphenyl (8)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 2-([1,1'-biphenyl]-4-yl)acetate (0.2878 g, 0.805 mmol, 1 equiv.), Ir(dF-ppy)₃ (5.2 mg, 0.008 mmol, 0.01 equiv.), triethylamine trihydrofluoride (391.2 μ L, 2.4 mmol, 3 equiv.), and DCM (4.00 mL, 0.2 M). Purified over silica with flash chromatography (10% ether in pentanes) to afford the title compound as a white solid (85.7 mg, 0.460 mmol, 57%). A second run with 1,3-dioxoisindolin-2-yl 2-([1,1'-biphenyl]-4-yl)acetate (0.2881 g, 0.806 mmol, 1 equiv.), Ir(dF-ppy)₃ (5.9 mg, 0.008 mmol, 0.01 equiv.), triethylamine trihydrofluoride (391.2 μ L, 2.4 mmol, 3 equiv.), and DCM (4.00 mL, 0.2 M) afforded 81.9 mg (0.440 mmol, 55%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.63 (d, *J* = 7.0 Hz, 2H), 7.60 (d, *J* = 7.1 Hz, 2H), 7.47 – 7.44 (m, 4H), 7.37 (t, 7.4, 2.0 Hz, 1H), 5.43 (d, *J* = 47.9 Hz, 2H).

¹³C NMR (126 MHz, Chloroform-*d*): 141.90 (d, *J* = 3.2 Hz), 140.75, 135.26 (d, *J* = 17.0 Hz), 128.98, 128.22 (d, *J* = 5.7 Hz), 127.69, 127.52, 127.31, 84.56 (d, *J* = 166.0 Hz).

¹⁹F NMR (376 MHz, Chloroform-*d*): δ -206.32 (t, *J* = 47.8 Hz).

HRMS: (EI-TOF) calculated for C₁₃H₁₁F⁺ [*M*⁺]: 186.08387, found 186.08393.

FTIR (thin film, cm⁻¹): ν 3057 (w), 3034 (w), 2954 (w), 2892 (w), 1613 (w), 1566 (w), 1486 (m), 1465 (w), 1406 (m), 1376 (m), 1222 (m), 1183 (w), 1157 (w), 1125 (w), 1024 (w), 970 (m), 947 (m), 846 (m), 821 (m), 758 (s), 730 (s), 689 (s), 601 (m), 548 (w), 489 (m).

1-(fluoromethyl)-4-iodobenzene (9)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 2-(4-iodophenyl)acetate (0.3270 g, 0.803 mmol, 1 equiv.), Ir(dF-ppy)₃ (3.5 mg, 0.005 mmol, 0.01 equiv.), triethylamine trihydrofluoride (391.2 μ L, 2.4 mmol, 3 equiv.), and DCM (4.00 mL, 0.2 M). Purified over silica with flash chromatography (5% ether in hexanes) to afford the title compound as a white solid contaminated with 6 mol% of 1,2-bis(4-iodophenyl)ethane (adjusted for bibenzyl, 109.3 mg, 0.463 mmol, 58%). A second run with 1,3-dioxoisindolin-2-yl 2-(4-iodophenyl)acetate (0.2523 g, 0.620 mmol, 1 equiv.), Ir(dF-ppy)₃ (3.1 mg, 0.004 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M) afforded 90.6 mg (0.384 mmol, 62% yield, adjusted for 6% 1,2-bis(4-iodophenyl)ethane contaminant).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.73 (d, *J* = 7.9 Hz, 2H), 7.12 (d, *J* = 6.5 Hz, 2H), 5.32 (d, *J* = 47.5 Hz, 2H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 137.88, 135.94 (d, *J* = 17.4 Hz), 129.28 (d, *J* = 6.0 Hz), 94.63 (d, *J* = 3.7 Hz), 83.99 (d, *J* = 167.4 Hz).

¹⁹F NMR (376 MHz, Chloroform-*d*): δ -208.94 (t, *J* = 47.4 Hz).

HRMS: (EI-TOF) calculated for C₇H₆FI⁺ ([*M*⁺]): 235.94927, found 235.95047.

Characterization data matched literature.¹³

1-(benzyloxy)-4-(fluoromethyl)benzene (10)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 2-(4-(benzyloxy)phenyl)acetate (0.2340 g, 0.604 mmol, 1 equiv.), Ir(dF-ppy)₃ (5.1 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M). Purified over silica with flash chromatography (10% ether in pentanes) to afford the title compound as a white solid (101.1 mg, 0.468 mmol, 77%). A second run with 1,3-dioxoisindolin-2-yl 2-(4-(benzyloxy)phenyl)acetate (0.2358 g, 0.609 mmol, 1 equiv.), Ir(dF-ppy)₃ (4.5 mg, 0.006

mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M) afforded 98.4 mg (0.455 mmol, 75% yield).

Note: This material decomposes in matter of hours to a purple solid if not kept rigorously dry.

¹H NMR (500 MHz, Chloroform-*d*): δ 7.46 (d, *J* = 7.2 Hz, 2H), 7.42 (t, *J* = 7.4 Hz, 2H), 7.38 – 7.33 (m, 3H), 7.02 (d, *J* = 8.2 Hz, 2H), 5.30 (d, *J* = 48.6 Hz, 2H), 5.11 (s, 2H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 159.45 (d, *J* = 3.4 Hz), 136.88, 130.00 (d, *J* = 5.0 Hz), 128.77, 128.77, 128.19, 127.59, 115.07 (d, *J* = 2.1 Hz), 84.67 (d, *J* = 164.5 Hz), 70.17.

¹⁹F NMR (282 MHz, Chloroform-*d*): δ -199.59 (t, *J* = 48.6 Hz).

HRMS: (EI-TOF) calculated for C₁₄H₁₃FO⁺ [*M*⁺]: 216.09449, found 216.09451.

FTIR (thin film, cm⁻¹): ν 2916 (w), 1805 (w), 1781 (m), 1738 (s), 1606 (w), 1515 (w), 1493 (m), 1465 (m), 1435 (w), 1410 (w), 1372 (m), 1349 (m), 1327 (m), 1274 (w), 1244 (w), 1212 (m), 1183 (m), 1124 (m), 1103 (s), 1077 (s), 1012 (m), 971 (s), 924 (m), 876 (s), 861 (m), 800 (m), 787 (m), 754 (s), 712 (m), 693 (s), 596 (m), 566 (m), 518 (m), 503 (s), 478 (m).

(4-(fluoromethyl)phenyl)(methyl)sulfane (11)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 2-(4-(methylthio)phenyl)acetate (0.333 g, 1.02 mmol, 1 equiv.), Ir(dF-ppy)₃ (7.4 mg, 0.01 mmol, 0.01 equiv.), triethylamine trihydrofluoride (489 μ L, 3.0 mmol, 3 equiv.), and DCM (5 mL, 0.2 M). Purified over silica with flash chromatography (3% ether in pentanes) to afford the title compound as a white solid contaminated with 5 mol% of 1,2-bis(4-(methylthio)phenyl)ethane (adjusted for bibenzyl, 99.0 mg, 0.634 mmol, 63%). A second run with 1,3-dioxoisindolin-2-yl 2-(4-(methylthio)phenyl)acetate (0.3288 g, 1.00 mmol, 1 equiv.), Ir(dF-ppy)₃ (8.1 mg, 0.01 mmol, 0.01 equiv.), triethylamine trihydrofluoride (489 μ L, 3.0 mmol, 3 equiv.), and DCM (5.00 mL, 0.2 M) afforded 93.8 mg (60% yield, 0.600 mmol, adjusted for 5% bibenzyl).

¹H NMR (500 MHz, Methylene Chloride-*d*₂): δ 7.31 (dd, *J* = 8.4, 2.1 Hz, 2H), 7.27 (dd, *J* = 7.8, 1.1 Hz, 2H), 5.31 (d, *J* = 48.2 Hz, 2H), 2.49 (s, 3H).

¹³C NMR (126 MHz, Methylene Chloride-*d*₂): δ 140.33 (d, *J* = 3.8 Hz), 133.30 (d, *J* = 17.0 Hz), 128.97 (d, *J* = 5.5 Hz), 126.67 (d, *J* = 1.7 Hz), 84.94 (d, *J* = 164.6 Hz), 15.82.

¹⁹F NMR (282 MHz, Chloroform-*d*): δ -204.39 (t, *J* = 48.0 Hz).

HRMS: (EI-TOF) calculated for C₈H₉FS⁺ [*M*⁺]: 156.04035, found 156.04705.

FTIR (thin film, cm⁻¹): ν 2921 (w), 1603 (m), 1495 (s), 1437 (m), 1406 (m), 1375 (m), 1219 (w), 1093 (m), 969 (s), 837 (m), 802 (s).

N-(4-(fluoromethyl)phenyl)acetamide (12)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 2-(4-acetamidophenyl)acetate (0.2732 g, 0.808 mmol, 1 equiv.), Ir(dF-ppy)₃ (4.8 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (391.2 μ L, 2.4 mmol, 3 equiv.), and DCM (4.00 mL, 0.2 M). Purified over silica with flash chromatography (20% acetone in hexanes) to afford the title compound as a cream white solid (98.7 mg, 0.590 mmol, 73%). A second run with 1,3-dioxoisindolin-2-yl 2-(4-acetamidophenyl)acetate (0.2730 g, 0.807 mmol, 1 equiv.), Ir(dF-ppy)₃ (4.9 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (391.2 μ L, 2.4 mmol, 3 equiv.), and DCM (4.00 mL, 0.2 M) afforded 98.5 mg (0.589 mmol, 73% yield).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.56 (d, *J* = 8.1 Hz, 2H), 7.36 (dd, *J* = 8.5, 2.0 Hz, 2H), 7.33 (broad s, 1H), 5.35 (d, *J* = 48.1 Hz, 2H), 2.21 (s, 3H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 168.64, 138.55 (d, *J* = 3.3 Hz), 132.05 (d, *J* = 17.3 Hz), 128.86 (d, *J* = 5.5 Hz), 119.94 (d, *J* = 1.1 Hz), 84.42 (d, *J* = 165.4 Hz), 24.75.

¹⁹F NMR (376 MHz, Chloroform-d): δ -203.91 (t, J = 48.1 Hz).

HRMS: (ESI-TOF) calculated for C₉H₁₁FNO⁺ [M+H]⁺: 168.08192, found 168.08186.

FTIR (thin film, cm⁻¹): ν 3296 (m), 3262 (m), 3192 (w), 3124 (w), 3042 (w), 2961 (m), 2903 (w), 1666 (s), 1598 (s), 1529 (s), 1512 (s), 1472 (s), 1410 (s), 1367 (s), 1315 (s), 1263 (s), 1218 (s), 1180 (s), 1165 (m), 1118 (m), 1036 (m), 1015 (m), 957 (s), 939 (s), 861 (s), 833 (s), 799 (s), 739 (s), 724 (s), 649 (s), 632 (s), 605 (s), 559 (s), 507 (s), 431 (m).

1-(fluoromethyl)-4-(trifluoromethoxy)benzene (13)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 2-(4-(trifluoromethoxy)phenyl)acetate (0.2285 g, 0.626 mmol, 1 equiv.), Ir(dF-ppy)₃ (5.7 mg, 0.008 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M). 1-Fluoronaphthalene (77.5 μ L, 0.600 mmol, 1 equiv.) was added, the reaction mixture was stirred, and an aliquot was removed and analyzed by ¹⁹F-NMR to obtain 64% yield of the title compound (0.401 mmol, 77.8 mg). A second run with 1,3-dioxoisindolin-2-yl 2-(4-(trifluoromethoxy)phenyl)acetate (0.2227 g, 0.610 mmol, 1 equiv.), Ir(dF-ppy)₃ (5.1 mg, 0.007 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M) afforded 56% ¹⁹F-NMR yield (relative to external 1-fluoronaphthalene, 0.342 mmol, 66.4 mg).

¹⁹F NMR (282 MHz, Chloroform-d): δ -58.61(s, 3F), -209.57 (t, J = 47.7 Hz, 1F).

HRMS: (EI-TOF) calculated for C₈H₆F₄O⁺ [M⁺]: 194.03493, found 194.03462.

This matched literature characterization.¹⁴

1-(fluoromethyl)-4-(trifluoromethyl)benzene (14)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 2-(4-(trifluoromethyl)phenyl)acetate (0.2132 g, 0.610 mmol, 1 equiv.), Ir(dF-ppy)₃ (4.4 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M). Fluorobenzene (56.5 μ L, 0.6 mmol, 1 equiv.) was added, the reaction mixture was stirred, and an aliquot was removed and analyzed by ¹⁹F-NMR to obtain 5% NMR yield (0.0305 mmol, 5.4 mg). A second run with 1,3-dioxoisindolin-2-yl 2-(4-(trifluoromethyl)phenyl)acetate (0.2149 g, 0.615 mmol, 1 equiv.), Ir(dF-ppy)₃ (4.7 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M) afforded 6% ¹⁹F-NMR yield (relative to external fluorobenzene, 0.0369 mmol, 6.6 mg).

¹⁹F NMR (282 MHz, Chloroform-d): δ -63.49 (s, 3F), -214.38 (t, J = 47.4 Hz, 1F), -63.18 (s, 3F, 1,2-bis(4-(trifluoromethyl)phenyl)ethane side product).

HRMS: (EI-TOF) calculated for C₈H₆F₄⁺ [M⁺]: 178.04001, found 178.04007.

5-(fluoromethyl)benzo[d][1,3]dioxole (15)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 2-(benzo[d][1,3]dioxol-5-yl)acetate (0.3241 g, 0.996 mmol, 1 equiv.), Ir(dF-ppy)₃ (5.2 mg, 0.0068 mmol, 0.01 equiv.), triethylamine trihydrofluoride (489 μ L, 3 mmol, 3 equiv.), and DCM (5.00 mL, 0.2 M). Purified over silica with flash chromatography (5% ether in pentanes) to afford the title compound as a colorless oil (93.1 mg, 0.604 mmol, 61%). A second run with 1,3-dioxoisindolin-2-yl 2-(benzo[d][1,3]dioxol-5-yl)acetate (0.3258 g, 1.00 mmol, 1 equiv.), Ir(dF-ppy)₃ (5.5 mg, 0.0072 mmol, 0.01 equiv.), triethylamine trihydrofluoride (489 μ L, 3 mmol, 3 equiv.), and DCM (5.00 mL, 0.2 M) afforded 103.8 mg (0.673 mmol, 65%).

¹H NMR (500 MHz, Methylene Chloride-*d*₂): δ 6.90 – 6.79 (m, 3H), 5.98 (s, 2H), 5.25 (d, *J* = 48.4 Hz, 2H).

¹³C NMR (126 MHz, Methylene Chloride-*d*₂): δ 148.75 (d, *J* = 3.4), 148.48 (d, *J* = 2.0 Hz), 130.54 (d, *J* = 17.0 Hz), 122.67 (d, *J* = 6.3 Hz), 109.09 (d, *J* = 4.6 Hz), 108.67 (d, *J* = 2.1 Hz), 102.02, 85.25 (d, *J* = 164.7 Hz).

¹⁹F NMR (376 MHz, Methylene Chloride-*d*₂): δ -199.76 (t, *J* = 48.4 Hz).

HRMS: (EI-TOF) calculated for C₈H₇FO₂⁺ [*M*⁺]: 154.04246, found 154.04333.

FTIR (thin film, cm⁻¹): ν 2962 (w), 2899 (m), 2783 (w), 1855 (w), 1609 (w), 1504 (s), 1491 (s), 1445 (s), 1380 (m), 1249 (s), 1198 (m), 1125 (m), 1100 (m), 1037 (m), 965 (s), 925 (s), 862 (s), 809 (s), 771 (s), 727 (m), 716 (m).

4-bromo-2-(fluoromethyl)thiophene (16)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 2-(4-bromothiophen-2-yl)acetate (0.2235 g, 0.610 mmol, 1 equiv.), Ir(dF-ppy)₃ (3.7 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μL, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M). 1-Fluoronaphthalene (26.0 μL, 0.200 mmol, 0.33 equiv.) was added, the reaction mixture was stirred, and an aliquot was removed and analyzed by ¹⁹F-NMR to obtain 41% ¹⁹F-NMR yield (0.250 mmol, 48.8 mg). A second run with 1,3-dioxoisindolin-2-yl 2-(4-bromothiophen-2-yl)acetate (0.2217 g, 0.605 mmol, 1 equiv.), Ir(dF-ppy)₃ (3.2 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μL, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M) afforded 40% ¹⁹F-NMR yield (0.242 mmol, 47.2 mg). Volatility of the of the title compound prevented clean isolation.

¹H NMR (500 MHz, Chloroform-*d*): δ 7.29 (d, *J* = 1.9 Hz, 1H), 7.07 (d, *J* = 2.4 Hz, 1H), 5.43 (d, *J* = 48.6 Hz, 2H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 144.45, 139.15 (d, *J* = 19.8 Hz), 131.12 (d, *J* = 5.7 Hz), 125.02 (d, *J* = 4.0 Hz), 77.94 (d, *J* = 169.0 Hz).

¹⁹F NMR (282 MHz, Chloroform-*d*): δ -193.56 (t, *J* = 48.7 Hz).

HRMS: (EI-TOF) calculated for C₄H₄⁷⁹BrFS⁺ [*M*⁺]: 195.91956, found 193.92077; calculated for C₄H₄⁸¹BrFS⁺ [*M*⁺]: 195.91743, observed 195.91854.

1-(cyclopentylfluoromethyl)-4-(trifluoromethyl)benzene (17)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 2-cyclopentyl-2-(4-(trifluoromethyl)phenyl)acetate (0.2588 g, 0.620 mmol, 1 equiv.), Ir(dF-ppy)₃ (2.7 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μL, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M). Purified over silica with flash chromatography (5% ether in hexanes) to afford the title compound as a colorless oil (138.2 mg, 0.561 mmol, 91%). A second run with 1,3-dioxoisindolin-2-yl 2-cyclopentyl-2-(4-(trifluoromethyl)phenyl)acetate (0.2565 g, 0.615 mmol, 1 equiv.), Ir(dF-ppy)₃ (3.3 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μL, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M) afforded 144.3 mg of the title compound (0.586 mmol, 95%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.63 (d, *J* = 8.1 Hz, 2H), 7.44 (d, *J* = 8.0 Hz, 2H), 5.27 (dd, *J* = 47.5, 7.5 Hz, 1H), 2.35 (dq, *J* = 18.5, 7.9 Hz, 1H), 1.80 (qd, *J* = 8.5, 7.8, 4.2 Hz, 1H), 1.71 – 1.61 (m, 2H), 1.61 – 1.47 (m, 4H), 1.37 – 1.24 (m, 1H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 144.25 (dd, *J* = 20.7, 1.4 Hz), 130.41 (qd, *J* = 32.4, 1.8 Hz), 126.39 (d, *J* = 7.0 Hz), 125.44 (q, *J* = 3.8 Hz), 124.18 (q, *J* = 272.1 Hz), 97.18 (d, *J* = 173.9 Hz), 46.10 (d, *J* = 22.0 Hz), 28.70 (d, *J* = 6.3 Hz), 28.48 (d, *J* = 2.4 Hz), 25.57 (d, *J* = 2.1 Hz).

¹⁹F NMR (376 MHz, Chloroform-*d*): δ -62.61 (s, 3F), -177.39 (dd, *J* = 47.6, 18.4 Hz).

HRMS: (ESI-TOF) calculated for C₁₃H₁₄F₄⁺ [*M*⁺]: 246.10261, found 246.10295.

FTIR (thin film, cm⁻¹): ν 2957 (w), 2872 (w), 1622 (w), 1452 (w), 1418 (w), 1323 (s), 1163 (s), 1122 (s), 1066 (s), 1018 (s), 988 (m), 935 (m), 836 (s), 762 (m), 680 (w), 605 (m), 530 (w), 466 (w), 450 (w), 409 (m).

2-chloro-5-(1-fluoroethyl)pyridine (18)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 2-(6-chloropyridin-3-yl)propanoate (contaminated with trace 1,3-dioxo-2,3-dihydro-1*H*-inden-2-yl 2-(6-chloropyridin-3-yl)-2-methylpropanoate) (0.1981 g, 0.599 mmol, 1 equiv.), Ir(dF-ppy)₃ (4.8 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M). Purified over silica with flash chromatography (3 to 5% ether in hexanes) to afford the title compound as a clear oil (56.1 mg, 0.352 mmol, 59%) with 2-chloro-5-(2-fluoropropan-2-yl)pyridine as an impurity from dimethylation of the 2-chloropyridine-5-acetic acid starting material (3.2 mg, 5%). A second run with 1,3-dioxoisindolin-2-yl 2-(6-chloropyridin-3-yl)propanoate (0.1983 g, 0.600 mmol, 1 equiv.), Ir(dF-ppy)₃ (4.3 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), DCM (3 mL, 0.2 M) afforded 54.6 mg of the title compound (0.342 mmol, 57% yield) with 2-chloro-5-(2-fluoropropan-2-yl)pyridine as an impurity (3.1 mg, 5%).

¹H NMR (500 MHz, Methylene Chloride-*d*₂): δ 8.36 (s, 1H), 7.68 (dd, *J* = 8.4, 2.5 Hz, 1H), 7.36 (d, *J* = 8.4 Hz, 1H), 5.67 (dq, *J* = 47.2, 6.5 Hz, 2H), 1.64 (dd, *J* = 24.1, 6.6 Hz, 3H).

¹³C NMR (126 MHz, Methylene Chloride-*d*₂): δ 151.70, 147.52 (d, *J* = 6.9 Hz), 136.45 (d, *J* = 21.8 Hz), 136.42 (d, *J* = 6.1 Hz), 124.69, 88.93 (d, *J* = 168.6 Hz), 22.88 (d, *J* = 24.7 Hz).

¹⁹F NMR (282 MHz, Methylene Chloride-*d*₂): δ -170.28 (dq, *J* = 47.7, 24.0 Hz, 1F). 2-chloro-5-(2-fluoropropan-2-yl)pyridine: δ -138.73 (hept, *J* = 22.1 Hz, 1F).

HRMS: (EI-TOF) calculated for C₇H₇ClFN [M⁺]: 159.02456, found 159.02435.

FTIR (thin film, cm⁻¹): 2986 (w), 2932 (w), 1591 (w), 1568 (w), 1460 (s), 1377 (w), 1327 (n), 1289 (w), 1215 (w), 1141 (w), 1114 (s), 1069 (s), 1022 (n), 1005 (n), 931 (w), 882 (n), 834 (n), 795 (n), 742 (n), 666 (w), 632 (w), 549 (w), 521 (w), 433 (m), 414 (m).

3-fluoro-*N,N*-dimethyl-3-(naphthalen-2-yl)propanamide (19)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 4-(dimethylamino)-2-(naphthalen-2-yl)-4-oxobutanoate (0.2557 g, 0.614 mmol, 1 equiv.), Ir(dF-ppy)₃ (3.1 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M). Purified over silica with flash chromatography (5% acetone, 25-50% EtOAc in hexanes) to afford the title compound as a white solid (90.0 mg, 0.367 mmol, 60%). A second run with 1,3-dioxoisindolin-2-yl 4-(dimethylamino)-2-(naphthalen-2-yl)-4-oxobutanoate (0.2556 g, 0.6 mmol, 1 equiv.), Ir(dF-ppy)₃ (5.2 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), DCM (3.00 mL, 0.2 M) afforded 102.5 mg (0.418 mmol, 68% yield).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.89-7.82 (m, 4H), 7.53-7.48 (m, 3H), 6.22 (ddd, *J* = 46.6, 8.3, 4.3 Hz, 1H), 3.21 (ddd, *J* = 15.7, 14.4, 8.3 Hz, 1H), 3.00 (s, 3H), 2.98 (s, 3H), 2.81 (ddd, *J* = 30.7, 15.7, 4.4 Hz, 1H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 169.12 (d, *J* = 4.8 Hz), 137.16 (d, *J* = 19.7 Hz), 133.42, 133.18, 128.62, 128.29, 127.87, 126.57, 126.53, 124.91 (d, *J* = 8.1 Hz), 123.24 (d, *J* = 5.9 Hz), 91.78 (d, *J* = 171.0 Hz), 41.37 (d, *J* = 26.5 Hz), 37.56, 35.70.

¹⁹F NMR (282 MHz, Chloroform-*d*): δ -174.38 (ddd, *J* = 45.8, 30.5, 14.3 Hz, 1F).

HRMS: (ESI-TOF) calculated for C₁₅H₁₆FNNaO⁺ [M+Na]⁺: 268.11081, found 268.11055.

FTIR (thin film, cm⁻¹): ν 3058 (w), 2925 (w), 1629 (s), 1578 (m), 1496 (m), 1397 (s), 1348 (m), 1324 (m), 1258 (m), 1213 (w), 1174 (w), 1159 (m), 1143 (m), 1125 (m), 1059 (m), 1002 (s), 967 (w), 954 (m), 903 (m), 867 (m), 849 (m), 825 (s), 750 (s), 737 (m), 659 (w), 601 (w), 570 (m), 539 (w), 496 (w), 483 (s), 474 (s), 448 (w), 413 (w).

1-(azidomethyl)-4-(1-fluoroethyl)benzene (20)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 2-(4-(azidomethyl)phenyl)propanoate (0.2133 g, 0.609 mmol, 1 equiv.), Ir(dF-ppy)₃ (2.7 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4

μL , 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M). Purified over silica with flash chromatography (5 to 10% ether in hexanes) followed by preparatory-TLC to afford the title compound as a colorless oil (63.7 mg, 0.355 mmol, 58%). A second run with 1,3-dioxoisindolin-2-yl 2-(4-(azidomethyl)phenyl)propanoate (0.2145 g, 0.612 mmol, 1 equiv.), $\text{Ir}(\text{dF-ppy})_3$ (5.2 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μL , 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M) afforded 58.7 mg of the title compound (0.328 mmol, 54% yield).

^1H NMR (500 MHz, Chloroform-*d*): δ 7.38 (d, J = 7.8 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 5.64 (dq, J = 47.6, 6.4 Hz, 1H), 4.35 (s, 2H), 1.65 (dd, J = 23.9, 6.5 Hz, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*): δ 141.76 (d, J = 19.7 Hz), 135.50 (d, J = 2.1 Hz), 128.47, 125.83 (d, J = 6.7 Hz), 90.73 (d, J = 168.0 Hz), 54.58, 23.05 (d, J = 25.1 Hz).

^{19}F NMR (376 MHz, Chloroform-*d*): δ -167.77 (dq, J = 47.7, 23.9).

HRMS: (ESI-TOF) calculated for $\text{C}_9\text{H}_{11}\text{FN}^+$ [$\text{M}+\text{H}-\text{N}_2$] $^+$: 152.08700, found 152.08720.

FTIR (thin film, cm^{-1}): ν 2984 (w), 2931 (w), 2092 (s), 1515 (w), 1445 (w), 1421 (m), 1376 (m), 1342 (m), 1248 (m), 1214 (m), 1064 (m), 1020 (m), 1005 (m), 880 (m), 843 (m), 815 (m), 724 (m), 671 (m), 544 (m), 488(w), 442 (w).

(3-(1-fluoroethyl)phenyl)(phenyl)methanone (21)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 2-(3-benzoylphenyl)propanoate (0.2381 g, 0.596 mmol, 1 equiv.), $\text{Ir}(\text{dF-ppy})_3$ (4.7 mg, 0.006 mmol, 0.01 equiv), triethylamine trihydrofluoride (293.4 μL , 1.8 mmol, 3 equiv), and DCM (3.00 mL, 0.2 M). Purified over silica with flash chromatography (5% ether in pentanes) to afford the title compound as a clear oil (91.2 mg, 0.400 mmol, 67%). A second run with 1,3-dioxoisindolin-2-yl 2-(3-benzoylphenyl)propanoate (0.2415 g, 0.605 mmol, 1 equiv.), $\text{Ir}(\text{dF-ppy})_3$ (4.7 mg, 0.006 mmol, 0.01 equiv), triethylamine trihydrofluoride (293.4 μL , 1.8 mmol, 3 equiv.), and DCM (3 mL, 0.2 M) afforded 87.4 mg of the title compound (0.383 mmol, 63% yield).

^1H NMR (500 MHz, Chloroform-*d*): δ 7.83 – 7.77 (m, 3H), 7.74 (dt, J = 7.6, 0.9 Hz, 1H), 7.64 – 7.57 (m, 2H), 7.50 (td, J = 7.6, 3.5 Hz, 3H), 5.70 (dq, J = 47.5, 6.5 Hz, 1H), 1.67 (dd, J = 24.0, 6.5 Hz, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*): δ 196.60, 142.01 (d, J = 20.0 Hz), 137.95, 137.50, 132.74, 130.20, 130.08, 129.24 (d, J = 6.7 Hz), 128.65, 128.50, 126.81 (d, J = 6.9 Hz), 90.62 (d, J = 168.9 Hz), 23.13 (d, J = 25.0 Hz).

^{19}F NMR (376 MHz, Chloroform-*d*): δ -168.56 (dq, J = 47.7, 23.9 Hz, 1F).

HRMS: (ESI-TOF) calculated for $\text{C}_{15}\text{H}_{12}\text{FO}^+$ ($[\text{M}+\text{H}]^+$): 228.09449, found 228.09466.

FTIR (thin film, cm^{-1}): 3061 (w), 2982 (w), 2930 (w), 2360 (w), 1656 (s), 1596 (m), 1483 (w), 1446 (w), 1376 (w), 1343 (w), 1317 (m), 1271 (s), 1210 (s), 1178 (w), 1139 (w), 1065 (m), 1023 (w), 1009 (w), 999 (w), 968 (m), 955 (m), 910 (w), 885 (m), 819 (m), 783 (m), 719 (s), 698 (s), 644 (s), 615 (m), 525 (w), 477 (w), 439 (w).

(2-fluoropropan-2-yl)benzene (22)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 2-methyl-2-phenylpropanoate (0.1889 g, 0.611 mmol, 1 equiv.), $\text{Ir}(\text{dF-ppy})_3$ (4.3 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μL , 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M). Purified over silica with flash chromatography (5 to 10% ether in hexanes) to afford the title compound as a colorless oil (70.3 mg, 0.509 mmol, 83%). A second run with 1,3-dioxoisindolin-2-yl 2-methyl-2-phenylpropanoate (0.1883 g, 0.609 mmol, 1 equiv.), $\text{Ir}(\text{dF-ppy})_3$ (4.3 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μL , 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M) afforded 76.0 mg of the title compound (0.550 mmol, 90% yield).

^1H NMR (500 MHz, Chloroform-*d*): δ 7.42 – 7.34 (m, 3H), 7.29 (m, 1H), 7.27 (tt, J = 7.0, 1.6 Hz, 1H), 1.70 (d, J = 22.0 Hz, 6H).

^{13}C NMR (126 MHz, Chloroform-*d*): δ 145.97 (d, J = 21.9 Hz), 128.39 (d, J = 1.0 Hz), 127.37 (d, J = 1.4 Hz), 123.89 (d, J = 8.9 Hz), 112.55, 95.80 (d, J = 168.9 Hz), 29.44 (d, J = 25.8 Hz).

¹⁹F NMR (282 MHz, Chloroform-*d*): δ -137.40 (hept, J = 21.9 Hz).

HRMS: (EI-TOF) calculated for $C_9H_{11}F^+$ ($[M^*]^+$): 184.04496, found 184.04548.

FTIR (thin film, cm^{-1}): ν 3030 (w), 2984 (w), 1604 (w), 1496 (w), 1447 (w), 1383 (w), 1368 (w), 1279 (m), 1203 (w), 1156 (w), 1104 (w), 1074 (w), 1030 (w), 939 (m), 912 (w), 851 (m), 762 (s), 697 (s), 552 (m), 467 (w), 405 (w). This matched literature characterization.¹⁵

Synthesized according to general procedure D with 1,3-dioxoisindolin-2-yl (2-phenylpropan-2-yl) oxalate (71.7 mg of material, 0.177 mmol, 1 equiv.), *note:* this material was determined to contain 38% 2-phenyl-2-propanol starting material), Ir(dF-ppy)₃ (1.7 mg, 0.002 mmol, 0.01 equiv.), triethylamine trihydrofluoride (97.8 μ L, 0.6 mmol, 3 equiv.), and DCM (1.00 mL, 0.2 M). 1-Fluoronaphthalene (26.0 μ L, 0.200 mmol, 1 equiv.) was added, the reaction mixture was stirred, and an aliquot was removed and analyzed by ¹⁹F-NMR to obtain 55% ¹⁹F-NMR yield of the title compound (0.0980 mmol, 13.5 mg). A second run with 1,3-dioxoisindolin-2-yl (2-phenylpropan-2-yl) oxalate (71.1 mg, 0.176 mmol, 1 equiv.), Ir(dF-ppy)₃ (1.5 mg, 0.002 mmol, 0.01 equiv.), triethylamine trihydrofluoride (97.8 μ L, 0.6 mmol, 3 equiv.), and DCM (1.00 mL, 0.2 M) afforded 54% ¹⁹F-NMR yield of the title compound (0.0940 mmol, 13.0 mg).

¹⁹F NMR (282 MHz, Methylene Chloride-*d*₂): δ -137.10 (heptet, J = 22.0 Hz, 1F).

Sample calculations for yield determination:

$$\begin{aligned} \text{Material mass} &= MW_{\text{oxalate}} \text{Moles}_{\text{oxalate}} + \text{Mole Fraction}_{\text{Impurity}} MW_{\text{Impurity}} \text{Moles}_{\text{oxalate}} \\ 71.7 \text{ mg} &= 353.33 \frac{\text{g}}{\text{mol}} X_{\text{oxalate}} + 0.38 \times 136.19 \frac{\text{g}}{\text{mol}} X_{\text{oxalate}} \\ 71.7 \text{ mg} &= 405.08 \frac{\text{g}}{\text{mol}} X_{\text{oxalate}} \\ 0.177 \text{ mmol} &= X_{\text{oxalate}} \end{aligned}$$

¹⁹F-NMR integration relative to 1-fluoronaphthalene as above is 1:0.49.

$$\begin{aligned} \text{Yield} &= \frac{\text{Actual mmol}}{\text{Theoretical mmol}} = \frac{0.200 \text{ mmol} \times 0.49}{0.177 \text{ mmol}} \\ \text{Yield} &= \frac{0.0980 \text{ mmol}}{0.177 \text{ mmol}} = 55\% \text{ yield} \end{aligned}$$

1-chloro-4-(1-fluorocyclohexyl)benzene (23)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 1-(4-chlorophenyl)cyclohexane-1-carboxylate (0.2352 g, 0.613 mmol, 1 equiv.), Ir(dF-ppy)₃ (2.7 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M). Purified over silica with flash chromatography (5 to 10% ether in hexanes) to afford the title compound as a colorless oil with 4% contamination with the styrene side product (114.8 mg, 0.540 mmol, 88%). A second run with 1,3-dioxoisindolin-2-yl 1-(4-chlorophenyl)cyclohexane-1-carboxylate (0.2331 g, 0.607 mmol, 1 equiv.), Ir(dF-ppy)₃ (3.2 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M) afforded 123.0 mg of the title compound (0.578 mmol, 95% yield) contaminated with 3% of the styrenal side product present.

Note: the alkyl fluoride undergoes complete conversion to the corresponding styrene overnight at room temperature in $CDCl_3$.

¹H NMR (500 MHz, Chloroform-*d*): δ 7.34 (s, 4H), 2.07–1.97 (m, 2H), 1.87–1.66 (m, 7H), 1.33 (m, 1H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 144.61 (d, J = 22.3 Hz), 133.13 (d, J = 1.9 Hz), 128.48 (d, J = 0.9 Hz), 125.60 (d, J = 9.4 Hz), 95.85 (d, J = 174.3 Hz), 37.24 (d, J = 23.8 Hz), 25.00, 22.01 (d, J = 1.6 Hz).

¹⁹F NMR (376 MHz, Chloroform-*d*): δ -158.55 (broad s, 1F).

HRMS: (ESI-TOF) calculated for $C_{12}H_{14}^{35}ClF^+$ ($[M^*]^+$): 212.07626, found 212.07627;

(ESI-TOF) calculated for $C_{12}H_{14}^{37}ClF^+$ ($[M^*]^+$): 214.07354, found 214.07364.

FTIR (thin film, cm⁻¹): ν 2933 (s), 2854 (m), 1489 (m), 1449 (m), 1437 (m), 1427 (m), 1398 (m), 1365 (w), 1351 (w), 1339 (w), 1258 (w), 1220 (w), 1149 (w), 1139 (w), 1103 (w), 1091 (s), 1034 (m), 1009 (s), 946 (s), 924 (m), 907 (s), 841 (s), 830 (m), 817 (s), 769 (m), 734 (s), 714 (m), 677 (m), 630 (w), 535 (s), 516 (m), 481 (s), 449 (m), 412 (w).

1-chloro-4-(1-fluorocyclopentyl)benzene (24)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 1-(4-chlorophenyl)cyclopentane-1-carboxylate (0.2266 g, 0.613 mmol, 1 equiv.), Ir(dF-ppy)₃ (2.9 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M). The product was not isolable as it decomposed in less than 5 minutes when neat. 1-Fluoronaphthalene (77.5 μ L, 0.600 mmol, 1 equiv.) was added, the reaction mixture was stirred, and an aliquot was removed and analyzed by ¹⁹F-NMR to obtain 85% ¹⁹F-NMR yield (0.521 mmol, 103.5 mg). A second run with 1,3-dioxoisindolin-2-yl 1-(4-chlorophenyl)cyclopentane-1-carboxylate (0.2263 g, 0.612 mmol, 1 equiv.), Ir(dF-ppy)₃ (3.0 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M) afforded 85% NMR yield by ¹⁹F-NMR (relative to external 1-fluoronaphthalene, 0.520 mmol, 103.3 mg).

¹⁹F NMR (470 MHz, Chloroform-*d*): δ -141.30 (tt, J = 37.4, 21.0 Hz).

HRMS: (EI-TOF) calculated for C₁₀H₁₀³⁵ClF⁺ ([M*]⁺): 198.06061, found 198.06093.

(EI-TOF) calculated for C₁₀H₁₀³⁷ClF⁺ ([M*]⁺): 200.05785, found 200.05799.

1-chloro-4-(1-fluorocyclobutyl)benzene (25)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 1-(4-chlorophenyl)cyclobutane-1-carboxylate (0.2150 g, 0.604 mmol, 1 equiv.), Ir(dF-ppy)₃ (2.1 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), DCM (3.00 mL, 0.2 M). Purified over silica with flash chromatography (5 to 10% ether in hexanes) to afford the title compound as a colorless oil (101.2 mg, 0.548 mmol, 91%). A second run with 1,3-dioxoisindolin-2-yl 1-(4-chlorophenyl)cyclobutane-1-carboxylate (0.2264 g, 0.636 mmol, 1 equiv.), Ir(dF-ppy)₃ (2.8 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M) afforded 105.2 mg of the title compound (0.570 mmol, 89% yield).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.43 (d, J = 8.4 Hz, 2H), 7.39 (d, J = 8.5 Hz, 2H), 2.68 (dddd, J = 21.3, 13.4, 10.1, 7.7 Hz, 2H), 2.55 (dddd, J = 15.1, 13.5, 8.7, 5.0 Hz, 2H), 2.11 (dddt, J = 15.1, 10.1, 7.9, 5.0 Hz, 1H), 1.82–1.70 (m, 1H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 140.87 (d, J = 23.1 Hz), 133.88 (d, J = 2.7 Hz), 128.68, 126.23 (d, J = 7.2 Hz), 97.15 (d, J = 207.1 Hz), 35.32 (d, J = 23.3 Hz), 12.50 (d, J = 9.7 Hz).

¹⁹F NMR (470 MHz, Chloroform-*d*): δ -127.11 (tt, J = 21.8, 15.0 Hz).

HRMS: (EI-TOF) calculated for C₁₀H₁₀³⁵ClF⁺ ([M*]⁺): 184.04496, found 184.04548.

(EI-TOF) calculated for C₁₀H₁₀³⁷ClF⁺ ([M*]⁺): 186.04217, found 186.04258.

FTIR (thin film, cm⁻¹): ν 2995 (w), 2946 (w), 1601 (w), 1494 (s), 1459 (w), 1419 (w), 1400 (w), 1306 (m), 1247 (m), 1134 (m), 1093 (s), 1063 (m), 1013 (s), 942 (w), 880 (w), 827 (s), 735 (w), 717 (w), 631 (w), 536 (s), 446 (m), 404 (w).

2-chloro-5-(4-fluorotetrahydro-2H-pyran-4-yl)pyridine (26)

Synthesized according to general procedure D with 1,3-dioxoisindolin-2-yl 2-(6-chloropyridin-3-yl)propanoate (0.0781 g, 0.202 mmol, 1 equiv.), Ir(dF-ppy)₃ (2.0 mg, 0.002 mmol, 0.01 equiv.), triethylamine trihydrofluoride (97.8 μ L, 0.6 mmol, 3 equiv.), and DCM (1.00 mL, 0.2 M). 1-Fluoronaphthalene (26.0 μ L, 0.200 mmol, 1 equiv.) was added, the reaction mixture was stirred, and an aliquot was removed and analyzed by ¹⁹F-NMR to obtain 72% ¹⁹F-

NMR yield (0.145 mmol, 31.4 mg). A second run with 1,3-dioxoisindolin-2-yl 2-(6-chloropyridin-3-yl)propanoate (0.0776 g, 0.201 mmol, 1 equiv.), Ir(dF-ppy)₃ (1.8 mg, 0.002 mmol, 0.01 equiv.), triethylamine trihydrofluoride (97.8 μ L, 0.6 mmol, 3 equiv.), and DCM (1.00 mL, 0.2 M) afforded 68% ¹⁹F-NMR yield (relative to external 1-fluoronaphthalene, 0.136 mmol, 29.4 mg). Purification was accomplished via preparatory TLC using 30% EtOAc in hexanes (2% triethylamine additive).

¹H NMR (500 MHz, Chloroform-*d*): δ 8.42 (d, *J* = 2.6 Hz, 1H), 7.68 (dd, *J* = 8.3, 2.6 Hz, 1H), 7.35 (d, *J* = 8.4 Hz, 1H), 3.96 (dd, *J* = 12.0, 5.7 Hz, 2H), 3.87 (td, *J* = 12.0, 2.0 Hz, 2H), 2.12 (dddd, *J* = 40.0, 14.0, 12.4, 5.6 Hz, 2H), 1.95 – 1.90 (m, 2H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 151.17 (d, *J* = 1.9 Hz), 146.03 (d, *J* = 9.5 Hz), 138.60 (d, *J* = 22.4 Hz), 135.00 (d, *J* = 9.1 Hz), 124.20 (d, *J* = 1.2 Hz), 92.31 (d, *J* = 176.1 Hz), 63.52, 37.07 (d, *J* = 22.7 Hz).

¹⁹F NMR (282 MHz, Chloroform-*d*): δ -161.91 (tt, *J* = 39.2, 10.4 Hz, 1F).

HRMS: (ESI-TOF) calculated for C₁₀H₁₁ClFNO [M*]⁺: 215.05077, found 215.05114.

FTIR (thin film, cm⁻¹): ν 3102 (w), 3049 (w), 2964 (w), 2933 (w), 2870 (w), 2245 (w), 2224 (w), 2157 (w), 2143 (w), 2023 (w), 1588 (w), 1566 (w), 1459 (m), 1419 (w), 1386 (w), 1373 (w), 1357 (w), 1295 (w), 1243 (w), 1218 (w), 1158 (w), 1125 (w), 1101 (s), 1043 (w), 1016 (m), 1003 (w), 939 (w), 920 (w), 847 (w), 840 (m), 753 (w), 743 (w), 697 (w), 632 (w), 561 (w), 554 (w), 484 (w), 462 (w), 438 (w), 417 (w), 411 (w).

1-fluoroadamantane (27)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl-adamantane-1-carboxylate (0.1975 g, 0.607 mmol, 1 equiv.), Ir(dF-ppy)₃ (4.5 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M). 1-Fluoronaphthalene (26 μ L, 0.2 mmol, 0.33 equiv.) was added, the reaction mixture was stirred, and an aliquot was removed and analyzed by ¹⁹F-NMR to obtain 36% ¹⁹F-NMR yield (0.219 mmol, 33.7 mg). A second run with 1,3-dioxoisindolin-2-yl-adamantane-1-carboxylate (0.2806 g, XX mmol, 1 equiv.), Ir(dF-ppy)₃ (3.9 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), DCM (3 mL, 0.2 M) afforded 40% NMR yield.

¹⁹F NMR (282 MHz, Chloroform-*d*): δ -128.48 (s, 1F).

HRMS: (EI-TOF) calculated for C₁₀H₁₅F⁺ [(M*)⁺]: found 154.11523; observed 154.11554.

Characterization matched literature characterization.¹⁶

1-(tert-butyl)-4-(2-fluoro-2-methylpropyl)benzene (28)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 3-(4-(tert-butyl)phenyl)-2,2-dimethylpropanoate (0.3081 g, 0.812 mmol, 1 equiv.), Ir(dF-ppy)₃ (3.0 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (391.2 μ L, 2.4 mmol, 3 equiv.), and DCM (4.00 mL, 0.2 M). 1-Fluoronaphthalene (103.3 μ L, 0.800 mmol, 1.0 equiv.) was added, the reaction mixture was stirred, and an aliquot was removed and analyzed by ¹⁹F-NMR to obtain 78% ¹⁹F-NMR yield (0.633 mmol, 131.9 mg). A second run with 1,3-dioxoisindolin-2-yl 3-(4-(tert-butyl)phenyl)-2,2-dimethylpropanoate (0.3061 g, 0.807 mmol, 1 equiv.), Ir(dF-ppy)₃ (3.1 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (391.2 μ L, 2.4 mmol, 3 equiv.), and DCM (4.00 mL, 0.2 M) afforded 74% ¹⁹F-NMR yield of the title compound (0.597 mmol, 124.4 mg).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.31 (d, *J* = 8.3 Hz, 2H), 7.14 (d, *J* = 7.9 Hz, 2H), 2.88 (d, *J* = 20.4 Hz, 2H), 1.34 (d, *J* = 21.2 Hz, 6H), 1.31 (s, 9H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 149.44, 134.04 (d, *J* = 4.3 Hz), 130.16, 125.13, 95.61 (d, *J* = 167.6 Hz), 47.22 (d, *J* = 22.9 Hz), 34.53, 31.53, 26.76 (d, *J* = 24.4 Hz).

¹⁹F NMR (376 MHz, Chloroform-*d*): δ -136.72 (triplet of heptets, *J* = 21.2, 20.4 Hz, 1F).

HRMS: (ESI-TOF) calculated for C₁₄H₂₁F⁺ [M]⁺: 208.16218, found 208.16195.

4-(2-fluoro-2-methylpropyl)benzonitrile (29)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 3-(4-cyanophenyl)-2,2-dimethylpropanoate (0.2813 g, 0.808 mmol, 1 equiv.), Ir(dF-ppy)₃ (4.0 mg, 0.008 mmol, 0.01 equiv.), triethylamine trihydrofluoride (391.2 μ L, 2.4 mmol, 3 equiv.), and DCM (4.00 mL, 0.2 M). Purified over silica with flash chromatography (10% ether in pentanes) to afford the title compound as a colorless oil (73.1 mg, 0.412 mmol, 51%). A second run with 1,3-dioxoisindolin-2-yl 3-(4-cyanophenyl)-2,2-dimethylpropanoate (0.2806 g, 0.805 mmol, 1 equiv.), Ir(dF-ppy)₃ (3.9 mg, 0.008 mmol, 0.01 equiv.), triethylamine trihydrofluoride (391.2 μ L, 2.4 mmol, 3 equiv.), and DCM (4.00 mL, 0.2 M) afforded 70.3 mg of the title compound (0.397 mmol, 49%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.59 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 7.9 Hz, 2H), 2.95 (d, *J* = 21.5 Hz, 2H), 1.33 (d, *J* = 21.2 Hz, 6H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 142.65 (d, *J* = 2.1 Hz), 132.00, 131.27 (d, *J* = 1.6 Hz), 119.07, 110.69, 94.76 (d, *J* = 169.8 Hz), 47.60 (d, *J* = 22.5 Hz), 26.80 (d, *J* = 24.4 Hz).

¹⁹F NMR (376 MHz, Chloroform-*d*): δ -138.36 (triplet of heptets, *J* = 21.5, 21.2 Hz, 1F).

HRMS: (ESI-TOF) calculated for C₁₁H₁₃FN⁺ (M+H)⁺: 178.10265, found 178.10261.

FTIR (thin film, cm⁻¹): ν 2983 (m), 2935 (w), 2227 (s), 1610 (m), 1507 (m), 1459 (w), 1417 (w), 1386 (m), 1374 (s), 1334 (w), 1261 (m), 1224 (m), 1188 (m), 1140 (m), 1126 (s), 1022 (w), 974 (w), 894 (m), 869 (s), 850 (s), 823 (s), 762 (s), 744 (w), 695 (w), 569 (s), 534 (m), 515 (w), 467 (m), 444 (w), 428 (w).

2-((4-fluoro-4-methylpentyl)oxy)-1,4-dimethylbenzene (30)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (0.2449 g, 0.619 mmol, 1 equiv.), Ir(dF-ppy)₃ (3.3 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (4.00 mL, 0.2 M). Purified over silica on a 1000-micron preparatory plate (10% ether in pentanes) to afford the title compound as a colorless oil (86.9 mg, 0.387 mmol, 63%). A second run with 1,3-dioxoisindolin-2-yl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (0.2394 g, 0.605 mmol, 1 equiv.), Ir(dF-ppy)₃ (2.7 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (4.00 mL, 0.2 M) afforded 93.4 mg of the title compound (0.416 mmol, 69%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.02 (d, *J* = 7.4 Hz, 1H), 6.67 (d, *J* = 7.3 Hz, 1H), 6.64 (s, 1H), 3.97 (t, *J* = 6.1 Hz, 2H), 2.32 (s, 3H), 2.19 (s, 3H), 1.96 – 1.89 (m, 2H), 1.86 – 1.77 (m, 2H), 1.40 (d, *J* = 21.4 Hz, 6H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 157.07, 136.63, 130.45, 123.72, 120.86, 112.12, 95.63 (d, *J* = 165.2 Hz), 67.95, 38.12 (d, *J* = 23.1 Hz), 26.83 (d, *J* = 24.8 Hz), 24.33 (d, *J* = 5.0 Hz), 21.55, 15.91.

¹⁹F NMR (376 MHz, Chloroform-*d*): δ -138.52 (triplet of hept, *J* = 20.8, 20.6 Hz, 1F).

HRMS: (ESI-TOF) calculated for C₁₄H₂₂FO⁺ (M+H)⁺: 225.16492, found 225.16498.

FTIR (thin film, cm⁻¹): ν 2979 (m), 2923 (m), 2868 (w), 1615 (m), 1585 (m), 1558 (w), 1540 (w), 1510 (s), 1459 (w), 1414 (m), 1385 (m), 1373 (m), 1309 (m), 1285 (m), 1264 (s), 1217 (m), 1190 (w), 1157 (s), 1129 (s), 1046 (s), 1001 (m), 967 (w), 948 (w), 923 (w), 869 (m), 843 (w), 802 (s), 762 (m), 715 (w), 604 (w), 587 (m), 542 (w), 447 (m), 401 (w).

(6aR,6bS,8aS,11S,12aR,14aR,14bS)-11-fluoro-4,4,6a,6b,8a,11,14b-heptamethyl-1,2,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,14a,14b-octadecahydronicene-3,14-dione (31)

Synthesized according to general procedure D with 1,3-dioxoisindolin-2-yl (2*S*,4*aS*,6*aS*,6*bR*,12*aS*,12*bR*,14*bR*)-2,4*a*,6*a*,6*b*,9,9,12*a*-heptamethyl-10,13-dioxo-1,2,3,4,4*a*,5,6,6*a*,6*b*,7,8,8*a*,9,10,11,12,12*a*,12*b*,13,14*b*-icosahydricene-2-carboxylate (0.1225 g, 0.200 mmol, 1 equiv.), Ir(dF-ppy)₃ (2.0 mg, 0.002 mmol, 0.01 equiv.), triethylamine trihydrofluoride (97.8 μ L, 0.6 mmol, 3 equiv.), and DCM (1.00 mL, 0.2 M). 1-Fluoronaphthalene (26.0 μ L, 0.200 mmol, 1 equiv.) was added, the reaction mixture was stirred, and an aliquot was removed and analyzed by ¹⁹F-NMR to obtain 32% ¹⁹F-NMR yield of both diastereomers (1.14:1 d.r., 0.0639 mmol, 28.3 mg). A second run with 1,3-dioxoisindolin-2-yl (2*S*,4*aS*,6*aS*,6*bR*,12*aS*,12*bR*,14*bR*)-2,4*a*,6*a*,6*b*,9,9,12*a*-heptamethyl-10,13-dioxo-1,2,3,4,4*a*,5,6,6*a*,6*b*,7,8,8*a*,9,10,11,12,12*a*,12*b*,13,14*b*-icosahydricene-2-carboxylate (0.1225 g, 0.200 mmol, 1 equiv.), Ir(dF-ppy)₃ (1.6 mg, 0.002 mmol, 0.01 equiv.), triethylamine trihydrofluoride (97.8 μ L, 0.6 mmol, 3 equiv.), and DCM (1.00 mL, 0.2 M) afforded 32% NMR yield (1.14:1 d.r., 0.0639 mmol, 28.3 mg).

¹H NMR (500 MHz, Chloroform-*d*): (both diastereomers) δ 5.68 (s, 1H, major diastereomer), 5.63 (s, 1H, minor diastereomer), 2.99 – 2.90 (m, 1H, both diastereomers overlap), 2.67 – 2.58 (m, 1H, both diastereomers overlap), 2.44 (s, 1H, minor diastereomer), 2.42 (s, 1H, major diastereomer), 2.40 – 2.32 (m, 2H, both diastereomers overlap), 2.23 – 2.11 (m, 1H, both diastereomers overlap), 2.05 (dd, *J* = 13.5, 4.2 Hz, 1H, minor diastereomer), 1.98 (td, *J* = 13.5, 4.3 Hz, 1H, major diastereomer), 1.90 – 1.81 (m, 2H, both diastereomers overlap), 1.80 – 1.61 (m, 4H, both diastereomers overlap), 1.60 – 1.49 (m, 4H, both diastereomers overlap), 1.48 – 1.42 (m, 2H, both diastereomers overlap), 1.42 – 1.37 (m, 4H, both diastereomers overlap), 1.35 – 1.33 (m, 3H, both diastereomers overlap), 1.32 – 1.22 (m, 7H, both diastereomers overlap), 1.18 (s, 3H, major diastereomer), 1.17 (s, 3H, minor diastereomer), 1.10 (s, 7H, minor diastereomer), 1.06 (s, 7H, major diastereomer), 0.89 (s, 3H, major diastereomer), 0.88 (s, 3H, minor diastereomer).

¹³C NMR (126 MHz, Chloroform-*d*): (both diastereomers) δ 217.29, 217.24, 199.54, 199.48, 169.23, 168.28, 128.50, 128.46, 95.58 (d, *J* = 310.1 Hz), 94.23 (d, *J* = 310.9 Hz), 61.23, 61.16, 55.57, 55.43, 49.42 (d, *J* = 11.0 Hz), 47.93, 47.87, 46.39 (d, *J* = 0.75 Hz), 45.39, 45.36, 43.52, 43.45, 43.01 (d, *J* = 20.9 Hz), 42.09 (d, *J* = 22.6 Hz), 39.91, 39.82, 38.19 (d, *J* = 10.9 Hz), 36.84, 36.80, 35.33 (d, *J* = 2.1 Hz), 34.37, 34.32, 33.14 (d, *J* = 20.7 Hz), 32.68 (d, *J* = 1.7 Hz), 32.25, 32.21 (d, *J* = 2.4 Hz), 32.07, 31.75, 29.85, 28.24, 28.10 (d, *J* = 3.2 Hz), 27.78 (d, *J* = 25.0 Hz), 26.60, 26.59, 26.51, 26.49, 26.47, 26.05 (d, *J* = 1.2 Hz), 23.65, 23.46, 23.21 (d, *J* = 26.0 Hz), 21.56, 21.55, 18.93 (d), 18.68, 18.68, 15.82, 15.80.

¹⁹F NMR (282 MHz, Chloroform-*d*): δ -124.71 (qt, *J* = 22.8, 13.5 Hz, 1F, minor diastereomer), -154.69 – -155.24 (m, 1F, major diastereomer).

HRMS: (ESI-TOF) calculated for C₂₉H₄₂FO₂⁺ (M⁺-HF)⁺: 422.31793, found 422.31814.

FTIR (thin film, cm⁻¹): ν 2976 (m), 2250 (w), 2208 (w), 2192 (w), 2174 (w), 2159 (w), 2013 (w), 1983 (w), 1969 (w), 1954 (w), 1702 (w), 1658 (m), 1460 (w), 1386 (m), 1272 (w), 1206 (w), 1111 (w), 913 (s), 870 (w), 736 (s), 648 (w), 487 (w), 444 (w), 430 (w), 419 (w), 408 (w).

1-(tert-butyl)-4-(fluoromethoxy)benzene (32)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 2-(4-(tert-butyl)phenoxy)acetate (0.2194 g, 0.621 mmol, 1 equiv.), Ir(dF-ppy)₃ (2.3 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M). 1-Fluoronaphthalene (77.50 μ L, 0.600 mmol, 1.00 equiv.) was added, the reaction mixture was stirred, and an aliquot was removed and analyzed by ¹⁹F-NMR to obtain 26% ¹⁹F-NMR yield (0.161 mmol, 29.4 mg). A second run with 1,3-dioxoisindolin-2-yl 2-(4-(tert-butyl)phenoxy)acetate (0.2213 g, 0.626 mmol, 1 equiv.), Ir(dF-ppy)₃ (3.4 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M) afforded 29% ¹⁹F-NMR yield (0.182 mmol, 33.1 mg). Attempted isolation and purification by flash chromatography or preparatory TLC showed an inseparable and unidentifiable impurity.

¹H NMR (500 MHz, Chloroform-*d*): δ 7.36 (dd, *J* = 8.7, 1.8 Hz, 2H), 7.03 (dd, *J* = 8.8, 1.9 Hz, 2H), 5.70 (d, *J* = 54.9 Hz, 2H), 1.32 (s, 9H).

¹⁹F NMR (376 MHz, Chloroform-*d*): δ -147.96 (t, *J* = 55.0 Hz, 1F).

HRMS: (EI-TOF) calculated for C₁₁H₁₅FO⁺ (M⁺): 182.11014, found 182.10960.

This matches literature characterization.¹⁷

(4-bromophenyl)(fluoromethyl)sulfane (33)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 2-((4-bromophenyl)thio)acetate (0.2386 g, 0.608 mmol, 1 equiv.), Ir(dF-ppy)₃ (4.3 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M). Purified over silica with flash chromatography (100% hexanes) to afford the title compound as a whitish oil (74.2 mg, 0.336 mmol, 55%) with a dimer (1,2-bis((4-bromophenyl)thio)ethane) impurity (7.1 mg, 5%). A second run with 1,3-dioxoisindolin-2-yl 2-((4-bromophenyl)thio)acetate (0.2398 g, 0.611 mmol, 1 equiv.), Ir(dF-ppy)₃ (5.6 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M) afforded 67.9 mg of the title compound (0.307 mmol, 50%) with dimer impurity (6.5 mg, 5%, 1,2-bis((4-bromophenyl)thio)ethane).

¹H NMR (500 MHz, Chloroform-*d*): (5% dimer impurity denoted with *) δ 7.47 (d, *J* = 8.5 Hz, 2H), *7.39 (d, *J* = 8.6 Hz, 4H), 7.36 (d, *J* = 8.5 Hz, 2H), *7.12 (d, *J* = 8.6 Hz, 4H), 5.70 (d, *J* = 52.7 Hz, 2H), *2.47 (s, 4H).

¹³C NMR (126 MHz, Chloroform-*d*): (5% dimer impurity denoted with *) δ 133.53 (d, *J* = 2.9 Hz), 132.45, 132.37 (d, *J* = 2.3 Hz), *131.93, *128.25, 122.25 (d, *J* = 0.9 Hz), 88.40 (d, *J* = 217.2 Hz), *16.07.

¹⁹F NMR (282 MHz, Chloroform-*d*): δ -182.27 (t, *J* = 52.7 Hz, 1F).

HRMS: (ESI-TOF) calculated for C₇H₆BrFS⁺ [(M*)⁺]: 219.93521, found 219.93539.

FTIR (thin film, cm⁻¹): ν 2939 (w), 1565 (w), 1473 (s), 1427 (w), 1387 (m), 1320 (m), 1230 (w), 1199 (w), 1091 (s), 1068 (s), 1008 (s), 954 (s), 807 (s), 736 (s), 719 (s), 501 (m), 478 (s), 426 (w).

(3a*S*,4*S*,6*S*,6a*R*)-4-(benzyloxy)-6-fluoro-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxole (34)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl (3a*S*,4*S*,6*R*,6a*R*)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxole-4-carboxylate (0.2628 g, 0.598 mmol, 1 equiv.), Ir(dF-ppy)₃ (3.6 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M). Purified over silica with flash chromatography (10% ether in pentanes) to afford the title compound as a white solid (68.3 mg, 0.255 mmol, 42%, >20:1 d.r.). A second run with 1,3-dioxoisindolin-2-yl (3a*S*,4*S*,6*R*,6a*R*)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxole-4-carboxylate (0.2665 g, 0.606 mmol, 1 equiv.), Ir(dF-ppy)₃ (3.5 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M) afforded 73.3 mg of the title compound (0.273 mmol, 46% yield, >20:1 dr).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.39 – 7.28 (m, 5H), 5.84 (d, *J* = 60.5 Hz, 1H), 5.33 (d, *J* = 2.8 Hz, 1H), 4.87 (t, *J* = 6.0 Hz, 1H), 4.83 (d, *J* = 11.6 Hz, 1H), 4.75 (d, *J* = 5.7 Hz, 1H), 4.52 (d, *J* = 11.5 Hz, 1H), 1.44 (s, 3H), 1.31 (s, 3H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 136.75, 128.64, 128.48, 128.16, 116.04 (d, *J* = 227.0 Hz), 113.07 (d, *J* = 1.2 Hz), 109.20 (d, *J* = 1.9 Hz), 84.18 (d, *J* = 39.8 Hz), 83.58, 69.56, 26.29, 24.90.

¹⁹F NMR (470 MHz, Chloroform-*d*): δ -119.26 (ddd, *J* = 60.4, 6.4, 2.8 Hz, 1F).

HRMS: (EI-TOF) calculated for C₁₃H₁₄FO₄⁺ ([M-CH₃]⁺): 253.08706, found 253.08760.

FTIR (thin film, cm⁻¹): ν 2992 (w), 2980 (w), 2957 (w), 2937 (w), 1455 (w), 1379 (m), 1355 (m), 1276 (w), 1245 (w), 1209 (m), 1159 (m), 1123 (m), 1088 (s), 1057 (s), 1018 (s), 996 (s), 967 (s), 934 (s), 863 (s), 840 (m), 815 (s), 786 (m), 758 (s), 701 (s), 653 (w), 636 (m), 563 (m), 513 (m), 504 (m), 443 (m), 428 (w).

(4-chlorophenyl)(4-((2-fluoropropan-2-yl)oxy)phenyl)methanone (35)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate (0.2811 g, 0.606 mmol, 1 equiv.), Ir(dF-ppy)₃ (2.7 mg, 0.006 mmol, 0.01 equiv.), triethylamine

trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M). 1-Fluoronaphthalene (77.50 μ L, 0.600 mmol, 1.00 equiv.) was added, the reaction mixture was stirred, and an aliquot was removed and analyzed by ^{19}F -NMR to obtain 56% ^{19}F -NMR yield (0.339 mmol, 99.3 mg). A second run with 1,3-dioxoisindolin-2-yl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate (0.2788 g, 0.601 mmol, 1 equiv.), Ir(dF-ppy) $_3$ (2.1 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M) afforded 57% ^{19}F -NMR yield of the title compound (relative to 1-fluoronaphthalene, 0.343 mmol, 100.3 mg).

Note: this compound rapidly decomposes from a flocculant white solid (purification over silica via flash chromatography, 10% ether in hexanes) to a brown oily residue upon workup and purification (approx. 30 minutes at room temperature). This decomposition affords acetone as observed by ^1H -NMR.

^1H NMR (500 MHz, Chloroform-*d*): δ 7.77 (d, J = 8.7 Hz, 2H), 7.74 (d, J = 8.5 Hz, 2H), 7.46 (d, J = 8.4 Hz, 2H), 7.23 (d, J = 8.6 Hz, 2H), 1.66 (d, J = 17.4 Hz, 6H).

^{13}C NMR (126 MHz, Chloroform-*d*): δ 194.51, 157.73 (d, J = 1.9 Hz), 138.72, 136.07, 132.84, 131.75, 131.31, 128.65, 121.46 (d, J = 3.2 Hz), 115.69 (d, J = 220.9 Hz), 25.64 (d, J = 29.2 Hz).

^{19}F NMR (470 MHz, Chloroform-*d*): δ -89.95 (hept, J = 17.3 Hz, 1F).

HRMS: (ESI-TOF) calculated for $\text{C}_{25}\text{H}_{19}\text{ClNO}_6^+$ ($[\text{M}+\text{H}]^+$): 464.08954, found 464.08910.

3-fluoro-4-(4-(1-fluoroethoxy)phenoxy)benzonitrile (36)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 2-(4-(4-cyano-2-fluorophenoxy)phenoxy)propanoate (0.2691 g, 0.603 mmol, 1 equiv.), Ir(dF-ppy) $_3$ (4.6 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M). Purified over silica via flash chromatography (0 to 5% ether in hexanes) to afford the title compound as a clear oil (96.8 mg, 0.352 mmol, 58%). A second run with 1,3-dioxoisindolin-2-yl 2-(4-(4-cyano-2-fluorophenoxy)phenoxy)propanoate (0.2363 g, 0.529 mmol, 1 equiv.), Ir(dF-ppy) $_3$ (5.0 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M) afforded 77.8 mg of the title compound (0.283 mmol, 53%).

^1H NMR (500 MHz, Methylene Chloride-*d* $_2$): δ 7.47 (dd, J = 10.4, 2.0 Hz, 1H), 7.37 (dt, J = 8.6, 1.7 Hz, 1H), 7.11 (d, J = 9.1 Hz, 2H), 7.04 (d, J = 9.1 Hz, 2H), 6.91 (t, J = 8.4 Hz, 1H), 5.95 (dq, J = 62.8, 4.9 Hz, 1H), 1.65 (dd, J = 20.0, 4.9 Hz, 3H).

^{13}C NMR (126 MHz, Methylene Chloride-*d* $_2$): δ 154.17 (d, J = 2.6 Hz), 152.99 (d, J = 251.0 Hz), 150.60, 150.59 (d, J = 10.7 Hz), 130.08 (d, J = 3.9 Hz), 121.43, 121.14 (d, J = 21.4 Hz), 119.44 (d, J = 1.9 Hz), 119.17 (d, J = 1.6 Hz), 118.11 (d, J = 2.6 Hz), 108.87 (d, J = 216.6 Hz), 106.91 (d, J = 8.2 Hz), 21.40 (d, J = 24.9 Hz).

^{19}F NMR (282 MHz, Methylene Chloride-*d* $_2$): δ -116.18 (dq, J = 63.0, 19.9 Hz, 1F), -130.76 (t, J = 9.2 Hz, 1F).

HRMS: (EI-TOF) calculated for $\text{C}_{15}\text{H}_{12}\text{F}_2\text{NO}_2^+$ ($[\text{M}+\text{H}]^+$): 275.07524, found 275.07593

FTIR (thin film, cm^{-1}): ν 3076 (w), 3001 (w), 2943 (w), 2232 (w), 1722 (w), 1614 (w), 1584 (w), 1495 (s), 1446 (w), 1422 (w), 1402 (s), 1366 (w), 1280 (s), 1214 (s), 1190 (s), 1147 (m), 1117 (s), 1071 (s), 1011 (w), 944 (s), 845 (s), 800 (s), 763 (w), 737 (w), 710 (w), 625 (w), 613 (m), 578 (w), 536 (m), 475 (w), 452 (w), 426 (w).

4-(difluoromethyl)-1,1'-biphenyl (37)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 2-([1,1'-biphenyl]-4-yl)-2-fluoroacetate (0.2282 g, 0.608 mmol, 1 equiv.), Ir(dF-ppy) $_3$ (4.1 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M). Purified over silica via flash chromatography (5% ether in hexanes) to afford the title compound as a white solid (69.9 mg, 0.342 mmol, 56%). A second run with 1,3-dioxoisindolin-2-yl 2-([1,1'-biphenyl]-4-yl)-2-fluoroacetate (0.2251 g, 0.600 mmol, 1 equiv.), Ir(dF-ppy) $_3$ (4.6 mg,

0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M) afforded 75.1 mg of the title compound (0.368 mmol, 61%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.68 (d, J = 8.0 Hz, 2H), 7.59 (t, J = 7.8 Hz, 4H), 7.47 (t, J = 7.7 Hz, 2H), 7.39 (t, J = 7.3 Hz, 1H), 6.70 (t, J = 56.5 Hz, 1H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 143.85 (t, J = 2.0 Hz), 140.33, 133.34 (t, J = 22.4 Hz), 129.06, 128.05, 127.59, 127.40, 126.17 (t, J = 6.0 Hz), 114.89 (t, J = 238.5 Hz).

¹⁹F NMR (376 MHz, Chloroform-*d*): δ -110.39 (d, J = 56.7 Hz, 2F).

HRMS: (EI-TOF) calculated for C₁₅H₁₂F₂NO₂⁺ ([M*]⁺): 204.07451, found 204.07426.

FTIR (thin film, cm⁻¹): ν 3059 (m), 3037 (m), 2361 (m), 2334 (w), 1806 (s), 1613 (m), 1570 (m), 1486 (m), 1411 (m), 1376 (s), 1314 (m), 1257 (m), 1224 (s), 1200 (s), 1182 (m), 1125 (m), 1071 (s), 1019 (s), 1004 (s), 953 (s), 836 (s), 765 (s), 738 (s), 689 (s), 647 (s), 635 (s), 559 (s), 506 (m), 416 (m).

(1,2,2,2-tetrafluoro-1-methoxyethyl)benzene (38)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (0.2317 g, 0.611 mmol, 1 equiv.), Ir(dF-ppy)₃ (3.3 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M). 1-Fluoronaphthalene (77.5 μ L, 0.600 mmol, 1.00 equiv.) was added, the reaction mixture was stirred, and an aliquot was removed and analyzed by ¹⁹F-NMR to obtain 89% ¹⁹F-NMR yield (0.544 mmol, 113.2 mg). A second run with 1,3-dioxoisindolin-2-yl 3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (0.2342 g, 0.617 mmol, 1 equiv.), Ir(dF-ppy)₃ (4.2 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M) afforded 88% ¹⁹F-NMR yield of the title compound (relative to 1-fluoronaphthalene, 0.543 mmol, 113.1 mg).

¹⁹F NMR (282 MHz, Chloroform-*d*): δ -83.68 (d, J = 3.7 Hz, 3F), -134.00 (q, J = 3.9 Hz, 1F)

HRMS: (EI-TOF) calculated for C₉H₈F₄NO⁺ ([M*]⁺): 208.05058, found 208.05119.

This matched literature characterization.¹⁸

Lit. ¹H NMR: δ 7.51 (s, 5H), 3.83 (s, 3H).

Lit. ¹⁹F NMR: δ -83.8 (d, J = 3.52 Hz, 3F), -134.3 (q, J = 3.52 Hz, 1F).

9,9-difluoro-9H-fluorene (39)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl 9-fluoro-9H-fluorene-9-carboxylate (0.2283 g, 0.612 mmol, 1 equiv.), Ir(dF-ppy)₃ (4.9 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M). Purified over silica via flash chromatography (3-5% ether in hexanes) to afford the title compound as a yellow solid (68.9 mg, 0.341 mmol, 56%). A second run with 1,3-dioxoisindolin-2-yl 9-fluoro-9H-fluorene-9-carboxylate (0.2245 g, 0.601 mmol, 1 equiv.), Ir(dF-ppy)₃ (5.2 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M) afforded 57.7 mg of the title compound (0.285 mmol, 48%).

¹H NMR (500 MHz, Methylene Chloride-*d*₂): δ 7.63 (dd, J = 7.2, 1.8 Hz, 2H), 7.58 (dd, J = 7.6, 1.1 Hz, 2H), 7.47 (td, J = 7.6, 1.0 Hz, 2H), 7.34 (td, J = 7.5, 1.0 Hz, 2H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 139.57 (t, J = 5.0 Hz), 138.05 (t, J = 25.1 Hz), 132.16 (t, J = 1.1 Hz), 128.91 (t, J = 1.4 Hz), 123.91, 123.35 (d, J = 242.6 Hz), 120.50.

¹⁹F NMR (282 MHz, Methylene Chloride-*d*₂): δ -111.54 (s, 2F).

HRMS: (EI-TOF) calculated for C₁₃H₈F₂⁺ ([M*]⁺): 202.05886, found 202.05986.

FTIR (thin film, cm⁻¹): ν 3077 (w), 2920 (w), 2320 (w), 1962 (w), 1923 (w), 1886 (w), 1815 (w), 1610 (m), 1589 (m), 1491 (m), 1452 (s), 1310 (m), 1292 (m), 1256 (s), 1208 (s), 1164 (s), 1115 (m), 1048 (s), 1031 (s), 983 (s), 938 (s), 869 (m), 765 (s), 727 (s), 653 (s), 617 (s), 585 (s), 509 (m), 422 (s), 416 (s).

(3-fluoro-3-methylbutyl)benzene (40)

Synthesized according to general procedure E with 1,3-dioxoisindolin-2-yl (2-methyl-4-phenylbutan-2-yl) oxalate (0.2257 g, 0.592 mmol, 1 equiv.), Ir(dF-ppy)₃ (4.6 mg, 0.006 mmol, 0.01 equiv.), triethylamine trihydrofluoride (293.4 μ L, 1.8 mmol, 3 equiv.), and DCM (3.00 mL, 0.2 M). 1-Fluoronaphthalene (26.0 μ L, 0.200 mmol, 0.33 equiv.) was added, the reaction mixture was stirred, and an aliquot was removed and analyzed by ¹⁹F-NMR to obtain 33% ¹⁹F-NMR yield (0.136 mmol, 22.6 mg).

¹H NMR (300 MHz, Chloroform-*d*): δ 7.34 – 7.27 (m, 2H), 7.22 – 7.17 (m, 3H), 2.77 – 2.70 (m, 2H), 2.00 – 1.87 (dm, J = 19.3 Hz, 2H), 1.42 (d, J = 21.4 Hz, 6H).

¹³C NMR (75 MHz, Chloroform-*d*): δ 142.19, 128.58, 128.43, 126.00, 95.43 (d, J = 165.6 Hz), 43.50 (d, J = 22.9 Hz), 30.42 (d, J = 5.2 Hz), 26.84 (d, J = 24.8 Hz).

¹⁹F NMR (282 MHz, Chloroform-*d*): δ -138.83 (hept of triplets, J = 21.4, 19.3 Hz, 1F).

HRMS: (EI-TOF) calculated for C₁₁H₁₅F⁺ ([M*]⁺): 166.11523, found 166.11517.

FTIR (thin film, cm⁻¹): ν 3063 (w), 3027 (w), 2980 (w), 2936 (w), 2348 (w), 1604 (w), 1494 (w), 1453 (w), 1385 (w), 1373 (m), 1253 (w), 1211 (w), 1181 (w), 1138 (w), 1073 (w), 1031 (w), 884 (w), 826 (w), 766 (w), 739 (m), 697 (s), 591 (w), 518 (w), 496 (w), 457 (w), 417 (w), 407 (w).

Characterization matched literature precedent.¹⁹

VI. Mechanistic Studies

Stern-Volmer Quenching

Fluorescence measurements were obtained using septa-capped UV-Quartz cuvettes (10 mm pathlength, 4 polished windows) obtained from Starna Cells (Cat#: 3-Q-10-GL 14-S). Excitation was performed at 400 nm; fluorescence spectra were obtained from 420-600 nm.

In a nitrogen filled glovebox, using deaerated materials (triethylamine·3HF was sparged under nitrogen for 1 h prior to entering the glovebox; anhydrous DCM was obtained from a solvent purification system and sparged for 1 h prior to entering the glovebox), the following solutions were prepared:

Photocatalyst solution (0.0002 M):

To an oven dried scintillation vial with a stir bar was added Ir(dF-ppy)₃ (1.70 mg, 2.23x10⁻³ mmol). This was diluted with 10.8 mL of DCM and stirred until completely dissolved, producing a 2.06x10⁻⁴ M solution of Ir(dF-ppy)₃.

Phthalimide ester solution (0.004 M):

To an oven dried scintillation vial, equipped with a stir bar, was added naproxen phthalimide ester **1** (16.2 mg, 4.32x10⁻² mmol). This was diluted in 10.8 mL of DCM and stirred until completely dissolved, producing a colorless, 4.00x10⁻³ M solution of phthalimide ester **1**.

Triethylamine·3HF solution (0.004 M):

To an oven dried scintillation vial, equipped with a stir bar was added 10.8 mL of DCM. followed by of Triethylamine·3HF (7.0 μ L, 4.3x10⁻² mmol) was then added and stirred to produce a 4.0x10⁻³ M solution of triethylamine·3HF.

Following preparation of these solutions, the solutions were allocated to the cuvettes and fluorescence quenching was determined with individual quenchers triethylamine·3HF and phthalimide ester, as well as the reaction mixture:

Table S7. Fluorescence Quenching with Triethylamine·3HF.

Concentration in Quencher (mM)	Triethylamine·3HF		Ir(dF-ppy) ₃		DCM	Fluorescence	
	Stock solution aliquot (μ L)	Stock solution conc. (M)	Stock solution aliquot (μ L)	Stock solution conc. (M)	DCM aliquot (μ L)	Measured intensity at 480 nm (a.u.)	I ₀ /I at 480 nm
0	0	0.004	200	0.0002	1900	657.4334717	1
0.200	100	0.004	200	0.0002	1800	644.2330322	1.02049016
0.400	200	0.004	200	0.0002	1700	660.0245361	0.99607429
0.600	300	0.004	200	0.0002	1600	662.6502686	0.99212738
0.800	400	0.004	200	0.0002	1500	630.7843628	1.04224757
1.00	500	0.004	200	0.0002	1400	617.6901245	1.06434189
						Slope:	54.719
						Intercept:	0.992
						R ² :	0.489
						RMSE:	0.023

Table S8. Fluorescence Quenching with Phthalimide Ester.

Concentration in Quencher (mM)	Naproxen Phthalimide Ester		Ir(dF-ppy) ₃		DCM	
	Stock solution aliquot (μL)	Stock solution conc. (M)	Stock solution aliquot (μL)	Stock solution conc. (M)	DCM aliquot (μL)	
0	0	0.004	200	0.0002	1900	
0.200	100	0.004	200	0.0002	1800	
0.400	200	0.004	200	0.0002	1700	
0.600	300	0.004	200	0.0002	1600	
0.800	400	0.004	200	0.0002	1500	
1.00	500	0.004	200	0.0002	1400	

Concentration in Quencher (mM)	Fluorescence-Run 1		Fluorescence-Run 2		Fluorescence-Run 3	
	Measured intensity at 480 nm (a.u.)	I ₀ /I at 480 nm	Measured intensity at 480 nm (a.u.)	I ₀ /I at 480 nm	Measured intensity at 480 nm (a.u.)	I ₀ /I at 480 nm
0	645.4230957	1	614.459656	1	614.6759033	1
0.200	245.3461304	2.63066344	228.971756	2.69231512	221.5214081	2.77479233
0.400	163.0663605	3.95803950	145.791550	4.2999474	149.3206024	4.11648422
0.600	121.1813278	5.32609361	115.776840	5.47978551	115.0957718	5.34056025
0.800	94.12566376	6.85703633	- ^a	-	88.39720917	6.95356685
1.00	79.78944397	8.08907875	75.6037064, 77.5903778	8.3945959, 8.17668722	74.44662476	8.25659867
	Slope:	7070.4		7216.1		7149.1
	Intercept:	1.1083		1.1538		1.1658
	R ² :	0.998		0.998		0.998

^aIn this replication, the 1.00 mM concentration data point was inadvertently performed twice, and the 0.8 mM loading was skipped.

Table S9. Fluorescence Quenching with Reaction Mixture (**1** and Triethylamine·3HF).

Concentration in Quencher (mM)	Naproxen Phthalimide Ester		Triethylamine·3HF		Ir(dF-ppy) ₃		DCM
	Stock solution aliquot (μL)	Stock solution conc. (M)	Stock solution aliquot (μL)	Stock solution conc. (M)	Stock solution aliquot (μL)	Stock solution conc. (M)	DCM aliquot (μL)
0	0	0.004	0	0.004	200	0.0002	1800
0.200	100	0.004	100	0.004	200	0.0002	1600
0.400	200	0.004	200	0.004	200	0.0002	1400
0.600	300	0.004	300	0.004	200	0.0002	1200
0.800	400	0.004	400	0.004	200	0.0002	1000
1.00	500	0.004	500	0.004	200	0.0002	800

Concentration in Quencher (mM)	Fluorescence-Run 1		Fluorescence-Run 2	
	Measured intensity at 480 nm (a.u.)	I ₀ /I at 480 nm	Measured intensity at 480 nm (a.u.)	I ₀ /I at 480 nm
0	623.660390	1	625.824768	1
0.200	236.922119	2.63234324	241.048889	2.5625659
0.400	154.681686	4.03189514	150.061050	4.17046773
0.600	110.838532	5.62674668	111.429939	5.61630718
0.800	89.1032562	6.99929908	87.2636719	7.17165293
1.00	718322296	8.68217989	77.6254883	8.06210411

Slope:	7586.7	7211.8
Intercept:	1.0354	1.1636
R ² :	0.999	0.994

Figure S2. Compiled Fluorescence Quenching Graphs.

Note: Error bars are not observable on all points as they are smaller than the size of the points represented.

Discussion.

Based on the observed quenching and the close match between individual quencher and reaction mixture quenching, the naproxen phthalimide ester (**1**) interacts with the photocatalyst preferentially to triethylamine·3HF. As triethylamine·3HF is a reductive quencher, while phthalimide esters are oxidative quenchers, the observed interaction is indicative of oxidative quenching of the photocatalyst, providing further mechanistic support for the proposed strategy. The Stern-Volmer quenching rate constant is $4.7 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ (based on a literature lifetime²⁰ for Ir(dF-ppy)₃, $\tau=1570 \text{ ns}$). This approaches the bimolecular diffusion rate limit ($10^{10} \text{ M}^{-1} \text{ s}^{-1}$). Furthermore, no significant increase in quenching rate was observed in the presence of triethylamine·3HF indicating that a hydrogen bonding interaction was unlikely.²¹ However, the extremely low concentrations employed for Stern-Volmer analysis make it difficult to observe evidence of interaction between a potential hydrogen-bond donor and a phthalimide ester hydrogen-bond acceptor. This is particularly noteworthy as an acidic additive is necessary for conversion and reactivity (*vide infra*).

Quantum yield determination

The quantum yield was determined using an adaptation of procedures reported by Yoon²² and Knowles.²³

General information

Potassium ferrioxalate ($\text{K}_3\text{Fe}(\text{C}_2\text{O}_4)_3 \cdot 3\text{H}_2\text{O}$) was obtained from Alfa Aesar and used as received. Concentrated sulfuric acid (17.8 M) was obtained from VWR and used as received. A Kessil PR-160 440 nm lamp was used at 50% power.

Figure S3. Emission Spectra of Lamps Evaluated.

The following solutions were prepared:

Developer solution (0.5 M buffered sulfuric acid , 0.056 M phenanthroline):

To a 250-mL volumetric flask was added 56.23 g (0.4132 mol) of sodium acetate trihydrate (Aldrich) and 2.5023 g (0.01389 mol) of 1,10-phenanthroline (Aldrich). This was diluted with deionized water and 7.02 mL of concentrated sulfuric acid (17.8 M) was added. Following this, the solution was diluted to 250 mL using deionized water. This solution was stored in the dark to slow degradation.

0.05 M sulfuric acid stock solution:

To a 100-mL volumetric flask was added 90 mL of deionized water followed by 0.280 mL of concentrated sulfuric acid (17.8 M). The solution was then diluted to 100 mL with deionized water.

0.15 M Ferrioxalate solution:

To a 25-mL volumetric flask was added 1.8432 g of potassium ferrioxalate ($[\text{K}_3\text{Fe}(\text{C}_2\text{O}_4)_3 \cdot 3\text{H}_2\text{O}]$, $\text{mw} = 491.25 \text{ g/mol}$, 3.7521 mmol). *Note:* The potassium ferrioxalate was weighed as fast as possible and solutions were kept in the dark to minimize the amount of background decomposition. The volumetric flask was wrapped in aluminum foil and diluted with approx. 20 mL of 0.05 M sulfuric acid stock solution (see above). Following this, the volumetric flask was sonicated and shaken to dissolve all of the potassium ferrioxalate solid. During this, the flask was kept wrapped in aluminum foil to prevent any incident light and was visualized in a darkened room to check for complete solvation of the green solid. Following complete dissolution of the solid, the solution was diluted to 25 mL with 0.05 M sulfuric acid solution.

Calibration of light source using potassium ferrioxalate.

Using black, opaque electrical tape, a 1 cm by 1 cm quartz cuvette was taped on 2 sides to prevent side incident light and then partially taped across the front face to produce a constant aperture for photon flux through the cuvette. The cuvette was placed a fixed distance (approx. 3 cm) from the lamp. The cuvette was equipped with a stir bar stirred at 500 rpm. The vial was charged with 3 mL of 0.15 M potassium ferrioxalate solution as prepared above. A 20 μL aliquot of the solution was taken and diluted into 5 mL of developer solution. The developer solution vial with the aliquot was immediately wrapped with aluminum foil and set aside to let the iron ligate with phenanthroline to produce $\text{Fe}(\text{phen})_3^{2+}$ as a red-orange solution. The cuvette was then irradiated using the Kessil PR-160 lamp (440 nm) at 50% power. Aliquots (20 μL) were taken at 20 second intervals. Immediately following the dilution of each aliquot into 5 mL of developer solution, the vial containing the developer solution and aliquot was wrapped in aluminum foil to prevent additional incidence of light. After all of the aliquot/developer solutions were allowed to develop for 45 minutes to 1 hr and become red-orange while wrapped, the solutions were sequentially unwrapped from aluminum foil and quickly transferred to cuvettes. Absorbance spectra were obtained between 460 and 560 nm. The absorbance at 510 nm was used to determine the quantity and rate of production of $\text{Fe}(\text{phen})_3^{2+}$ ($\epsilon_{510 \text{ nm}} = 11,100 \text{ M}^{-1} \text{ cm}^{-1}$). This process was repeated in triplicate.

Figure S4. Cuvette for Quantum Yield Determination. The face of the cuvette (1 cm pathlength) towards the lamp has tape only above a certain threshold (approximately 2.5 cm so that several 20-75 μL aliquots could be taken).

Results and data analysis.

Figure S5. Replicates for $\text{Fe}(\text{phen})_3^{2+}$ Absorption.

Table S10. Absorption data of Fe(phen)_3^{2+} at 510 nm.

Time of Irradiation (s)	Run 1		Run 2		Run 3	
	Measured Absorbance (a.u.)	Δ Absorbance (a.u.)	Measured Absorbance (a.u.)	Δ Absorbance (a.u.)	Measured Absorbance (a.u.)	Δ Absorbance (a.u.)
0	0.303585678	0	0.341238111	0	0.381247968	0
20	0.543958962	0.240373284	0.513885617	0.172647506	0.654968739	0.273620771
40	0.759392679	0.455807	0.775179505	0.430556942	0.802574098	0.421326131
60	0.92545116	0.621865481	0.957174957	0.615936846	1.037086844	0.655838877
80	1.062799573	0.759213895	1.162686944	0.821448833	1.192298889	0.811050922
100	1.30434072	1.000755042	1.310974479	0.969736368	1.370225549	0.988977582
Linear regression R^2	–	0.990	–	0.995	–	0.988

Figure S6. Change in Relative Absorbance over Irradiation.

From this, the number of iron ions produced by ferrioxalate photodegradation may be determined:

Eq. S1

$$\text{moles } \text{Fe}^{2+} = \frac{\Delta \text{Abs}_{510 \text{ nm}} V_1 V_3}{\epsilon_{510 \text{ nm}} l V_2}$$

ΔAbs = difference in absorbance at 510 nm between sample and ‘blank’

l = path length of cuvette (1 cm)

$\epsilon_{510 \text{ nm}}$ = extinction coefficient of Fe(phen)_3^{2+} complex at 510 nm ($\epsilon = 11,100 \text{ M}^{-1} \text{ cm}^{-1}$)

V_1 = total volume of irradiated solution (3 mL at start and decreased with each aliquot)

V_2 = volume of aliquot taken from V_1 (20 μL)

V_3 = the volume that V_2 is diluted into (5 mL)

Table S11. Fe(phen)₃²⁺ Photochemical Production.

Time of Irradiation (s)	Run 1 Fe ²⁺ produced (x 10 ⁻⁵ mol)	Run 2 Fe ²⁺ produced (x 10 ⁻⁵ mol)	Run 3 Fe ²⁺ produced (x 10 ⁻⁵ mol)
0	0	0	0
20	1.61332	1.15876	1.83646
40	3.03871	2.87038	2.80884
60	4.11776	4.07850	4.34272
80	4.99303	5.40232	5.33394
100	6.53646	6.33386	6.45954

Figure S7. Fe(phen)₃²⁺ Photochemical Production Graph.

From these iron-phenanthroline complex production data, the total number of photons to pass through the cuvette can be determined as a function of time.

Eq. S2

$$\text{photons absorbed} = \frac{\text{mol of Fe}^{2+}}{\phi_{436 \text{ nm}} \times F}$$

$\phi_{436 \text{ nm}}$ = quantum efficiency for wavelength and concentration (1.012 at 0.15 M ferrioxalate solution²⁴)
 F = fraction of light absorbed by the ferrioxalate solution (absorbance of a 0.15 M potassium ferrioxalate solution is 2.8184 a.u. at 440 nm (from Absorption spectrum), implying that $F = 0.9985 \sim 1$ at 440 nm)

Eq. S3

$$F = 1 - 10^{-\text{Absorbance}_{440 \text{ nm}}}$$

$$F = 1 - 10^{-2.8184}$$

$$F = 0.9985$$

Figure S8. Absorption Spectrum for Potassium Ferrioxalate Solution.

Table S12. Determination of Photon Flux.

Time of Irradiation (s)	Run 1 Photons absorbed ($\times 10^{-5}$ einstein)	Run 2 Photons absorbed ($\times 10^{-5}$ einstein)	Run 3 Photons absorbed ($\times 10^{-5}$ einstein)
0	0	0	0
20	1.59685	1.14693	1.81772
40	3.0077	2.84108	2.78017
60	4.07573	4.03687	4.29839
80	4.94207	5.34718	5.27950
100	6.46975	6.26922	6.39361
Linear Regression fit slope ($\times 10^{-7}$)	6.54 ± 0.18	6.52 ± 0.13	6.67 ± 0.19
R^2	0.987	0.994	0.985
Photon flux ($\times 10^{-7}$ einsteins/s)	6.54 ± 0.18	6.52 ± 0.13	6.67 ± 0.19

Figure S9. Photon Absorption Graphs.

Figure S10. Compiled Photon Absorption Graphs.

The average photon flux is therefore $6.58 \pm 0.29 \times 10^{-7}$ Einstein s⁻¹.

Tracking light absorption of the reaction mixture.

The absorption spectrum of the photocatalyst was determined at catalytically relevant concentrations (0.002 M).

Figure S11. Absorbance Spectrum of Ir(dF-ppy)₃.

Based on the absorption spectrum ($Abs_{440\text{ nm}} = 1.9578$ a.u.), more than 98% of light at 440 nm was absorbed by the photocatalyst:

$$F = 1 - 10^{-Absorbance_{440\text{ nm}}}$$

$$F = 1 - 10^{-1.9578}$$

$$F = 0.989$$

Eq. S4

Using this, it was inferred that essentially all photon flux determined by actinometry was absorbed by the photocatalyst and negligible light passed through the cuvette unabsorbed or was absorbed by phthalimide ester **1**.

Notably, the phthalimide ester did not absorb significantly in the visible region at reaction concentrations. Moreover, no bathochromic shift was observed in the presence of a potential hydrogen bond donor like $\text{Et}_3\text{N}\cdot 3\text{HF}$. Further, the lack of reactivity in the absence of a photocatalyst is indicative that the reaction is photocatalyst mediated (see Figure 1).

Figure S12. Absorbance Spectrum of **1** with Added Triethylamine·3HF.

Time Course for Initial Rate.

The initial rate of the reaction was determined in duplicate:

To an oven dried scintillation vial with a stir bar was added $\text{Ir}(\text{dF-ppy})_3$ (16.3 mg, 0.0214 mmol, 0.01 eq.), 2-fluorobiphenyl (120.3 mg, 0.6986 mmol, 0.3322 eq.), and phthalimide ester **1** (789.3 mg, 2.103 mmol, 1 eq.). The vial was charged with 1.00 mL of triethylamine·3HF (6.13 mol, 2.92 eq.). The vial was frozen in a -78°C bath and subjected to three cycles of evacuation/backfill with nitrogen. Following this, the vial was removed and charged with 10.5 mL of dry, sparged DCM. The vial was stirred to dissolve all of the solids. Aliquots (3.00 mL) were taken from the vial and added to the cuvette (taped with electrical tape and located as during calibration) which was capped with a septa cap and under nitrogen via spaghetti line during the transfer. After the transfer, an aliquot (approximately 75 μL) was taken from the cuvette, diluted in approximately 400 μL of CDCl_3 and subjected to ^1H -decoupled, ^{19}F -NMR analysis to verify no product formation. Subsequently, the cuvette was irradiated using the calibrated Kessil PR160 440 nm (*vide supra*). Aliquots ($\sim 75 \mu\text{L}$) were taken at 1-minute intervals, diluted in $\sim 400 \mu\text{L}$ of CDCl_3 , and subjected to ^1H -decoupled, ^{19}F -NMR analysis to determine production rate of alkyl fluoride **2**.

Table S13. Initial Rate of Alkyl Fluoride **2** Production.

Time of Irradiation (s)	Run 1 Product yield ($\times 10^{-5}$ mmol)	Run 2 Product yield ($\times 10^{-5}$ mmol)
0	0	0
60	0.998	1.20
120	2.59	2.79
180	3.99	4.59
240	5.59	5.79
300	7.58	7.78
Linear regression fit slope ($\times 10^{-7}$)	2.377 ± 0.075	2.504 ± 0.052
R ²	0.986	0.994

Figure S13. Initial Rate for Alkyl Fluoride **2** Production.

Determination of Quantum Yield.

Using the average initial rate of alkyl fluoride production of 2.441×10^{-7} mol/s, the quantum yield was determined:

Eq. S5

$$\text{Quantum yield} = \frac{\text{Product rate}}{\text{Photon flux rate}} = \frac{2.441 \times 10^{-7} \text{ mol/s}}{6.58 \times 10^{-7} \text{ einstein/s}} = 0.37$$

This is indicative that the alkyl fluorination is likely not proceeding via a chain mechanism.

Discussion of Chain Mechanism.

Scheme S1. Potential Chain Mechanism Pathway.

As the photocatalyst absorbs almost all of the light—the photocatalyst has significantly higher extinction coefficients in the visible region compared to the phthalimide ester substrate (see absorbance spectra of **1** and Ir(dF-ppy)₃)—there is likely only a very small fraction of excited phthalimide ester substrate at any given time. This makes an excited state phthalimide ester unlikely to propagate a chain mechanism despite the greater concentration of the phthalimide ester substrate. An energy transfer mechanism to produce an excited state phthalimide ester is unlikely as the emission spectrum of Ir(dF-ppy)₃ (emission >450 nm) does not overlap with the absorption spectrum of the phthalimide ester (only absorbance <400 nm).

A ground state chain propagation mechanism is also unlikely on the basis of redox potentials. The literature potential for the reduction of *N*-hydroxyphthalimide esters is reported to be $E_{\text{red,peak}} = -1.28$ V vs. SCE in MeCN.²⁵ The literature oxidation potentials for benzylic and tertiary radicals meanwhile are reported to be 0.73 V and 0.09 V vs SCE, respectively.^{26,27} Therefore, reduction of the redox active ester by the radical species is thermodynamically disfavored by approximately 1.3-2.0 V. While there could be a significant shift in the reduction potential of the redox active ester to more positive potentials due to the presence of a hydrogen bond donor (triethylamine·3HF), no absorption shift was observed by UV-Vis spectroscopy (see above, Figure S11) nor was a significant increase in quenching rate observed in the presence of triethylamine·3HF (see Stern-Volmer quenching experiments in Tables S8, S9, and Figure S1).

Radical Trapping Experiments.

To determine the presence of radicals in this reaction, a variety of radical traps were evaluated with minor modifications. Following general procedure D, each radical trap was added prior to evacuation/backfill with nitrogen in the indicated amount.

Table S14. Styrene Trapping Experiments.

Expt.	Styrene equiv	% Yield ^a (A+B)	% Yield ^a A	% Yield ^a B
1	1.5	94	21	73
2	3.0	90	10	80

^aYields determined by ^1H -decoupled ^{19}F -NMR vs. external 1-fluoronaphthalene

Styrene is a well-known and utilized trap for radicals. However, styrene could also act as a competitive nucleophile. If a tertiary carbocation was formed, styrene may outcompete fluoride as a nucleophile for the initial carbocation and then fluoride may add to the resulting benzylic cation. While it is unlikely for styrene to be a competitive nucleophile for one carbocation over another, to probe whether styrene was acting as a nucleophile we varied the electronics of the styrene by using the para -OMe and -CN species. We anticipated that the more electron rich alkene would be more likely to serve as a nucleophile leading to a higher ratio of benzylic to tertiary fluoride. Conversely, with the electron poor alkene, we anticipated that the ratio would shift from the benzylic towards the tertiary fluoride. However, within error, we did not observe a significant difference in the relative ratios of product formation by varying the electronics of the styrene (Table S15). Therefore, we concluded that the styrene is more likely acting as a radical trap than as a nucleophile.

Table S15. Electronic Effect on Styrene Trapping.

Expt.	<i>p</i> -X-Styrene	Hammett (σ_p)	σ_p^+	σ_p^-	% Yield ^a (A+B)	% Yield ^a A	% Yield ^a B
1	<i>p</i> -CN	0.66	0.66	1.00	64	4	60
2	<i>p</i> -H	0.00	0.00	0.00	85	17	68
3	<i>p</i> -OMe	-0.27	-0.78	-0.26	64	8	56

^aYields determined by ^1H -decoupled ^{19}F -NMR vs. external 1-fluoronaphthalene

As the styrene trapping may be occurring via a cationic trapping mechanism, we also conducted the reaction using methyl acrylate (as a non-nucleophilic olefin) and TEMPO (2,2,6,6-Tetramethyl-1-piperidinyloxy) as radical traps.

Table S16. Trapping with Non-Styrene Radical Traps.

Expt.	Radical Trap	% Yield ^a A	Notes
1	None	75	-
2		45	 Detected by HRMS
3		Not detected	 Detected by HRMS

^aYields determined by ¹H-decoupled ¹⁹F-NMR vs. external 1-fluoronaphthalene

As the reaction efficiency is significantly diminished or even completely quenched in the presence of these radical traps, it was inferred that radicals were intermediates in the formation of the alkyl fluorides. Moreover, detection of radical trap adducts lends additional evidence that alkyl radicals are present.

1-((5-(2,5-dimethylphenoxy)-2-methylpentan-2-yl)oxy)-2,2,6,6-tetramethylpiperidine (42)

HRMS: (ESI-TOF) calculated for C₂₃H₄₀NO₂⁺ ([M+H]⁺): 362.30536, found 362.3057.

Methyl 7-(2,5-dimethylphenoxy)-4,4-dimethylheptanoate (43)

HRMS: (EI-TOF) calculated for C₁₈H₂₈O₃⁺ [M⁺]: 292.20330, found 292.20396.

2-((6-fluoro-4,4-dimethyl-6-phenylhexyl)oxy)-1,4-dimethylbenzene (44)

¹⁹F NMR (282 MHz, Chloroform-*d*): δ -171.30 (ddd, *J*=48.8, 40.5, 18.9).

HRMS: (EI-TOF) calculated for C₂₂H₂₉FO⁺ [M⁺]: 328.21970, found 328.22000.

2-((6-fluoro-4,4-dimethyl-6-phenylhexyl)oxy)-1,4-dimethylbenzene (S36)

¹⁹F NMR (282 MHz, Chloroform-*d*): δ -165.57 (ddd, J =48.6, 38.8, 18.5 Hz).

HRMS: (EI-TOF) calculated for $C_{23}H_{31}FO_2^+$ [(M-HF)⁺]: 338.22403, found 338.22511.

4-(6-(2,5-dimethylphenoxy)-1-fluoro-3,3-dimethylhexyl)benzonitrile (S37)

¹⁹F NMR (282 MHz, Chloroform-*d*): δ -176.82 (ddd, J =49.2, 42.0, 19.2 Hz).

HRMS: (ESI-TOF) calculated for $C_{23}H_{28}FNO^+$ [M⁺]: 353.21494, found 353.21565.

Carbocation Trapping Experiments.

To probe for evidence of a carbocation, a variety of nucleophiles were evaluated using small modifications to general procedure E and F with catalytic quantities of triethylamine trihydrofluoride. Intriguingly, we observed no conversion in the absence of triethylamine trihydrofluoride acid. This is likely due to the necessity of a Lewis- or Brønsted acid to interact with the phthalimide radical anion to prevent back electron transfer (BET) from the radical anion to the now oxidized photocatalyst (Ir^{IV}) and thereby facilitate irreversible fragmentation.

2-methoxy-6-(1-(2,4,6-trimethoxyphenyl)ethyl)naphthalene (45)

Synthesized according to general procedure E with minor alteration, with 1,3-dioxoisindolin-2-yl 2-(6-methoxynaphthalen-2-yl)propanoate (230.0 mg, 0.613 mmol, 1 equiv.), Ir(dF-ppy)₃ (3.6 mg, 0.0047 mmol, 0.007 equiv.), 1,3,5-trimethoxybenzene (307.3 mg, 1.83 mmol, 3 equiv.), catalytic triethylamine trihydrofluoride (10.0 μ L, 0.061 mmol, 0.1 equiv.), and DCM (3.00 mL, 0.2 M). Purified over silica with flash chromatography (0-15% EtOAc in hexanes) to afford the title compound as a white solid (0.1774 g, 0.503 mmol, 82%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.70 – 7.64 (m, 2H), 7.57 (d, J = 8.5 Hz, 1H), 7.36 (dd, J = 8.5, 1.9 Hz, 1H), 7.11 – 7.07 (m, 2H), 6.14 (s, 2H), 4.87 (q, J = 7.2 Hz, 1H), 3.90 (s, 3H), 3.80 (s, 3H), 3.68 (s, 6H), 1.73 (d, J = 7.2, 3H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 159.58, 159.20, 156.96, 142.03, 132.66, 129.31, 129.03, 127.64, 125.85 (2 carbon signals overlap), 124.73, 118.17, 115.95, 105.63, 91.54, 55.91, 55.38, 33.02, 17.91.

HRMS: (EI-TOF) calculated for $C_{22}H_{25}O_4^+$ [(M+H)⁺]: 353.17474, found 353.17546.

FTIR (thin film, cm⁻¹): ν 2935 (m), 2834 (m), 1602 (s), 1591 (s), 1502 (m), 1490 (m), 1449 (s), 1436 (m), 1413 (m), 1389 (m), 1362 (m), 1330 (m), 1260 (m), 1218 (s), 1203 (s), 1192 (s), 1178 (m), 1162 (m), 1150 (s), 1116 (s), 1070 (m), 1053 (s), 1036 (s), 988 (m), 952 (m), 924 (m), 884 (s), 854 (s), 817 (s), 782 (m), 768 (m), 748 (m), 731 (m), 703.8 (m), 656 (m), 632 (m), 612 (m), 515 (m), 501 (m), 476 (s), 459 (m).

2-methoxy-6-(1-phenoxyethyl)naphthalene (46)

Synthesized according to general procedure E with minor alteration, with 1,3-dioxoisindolin-2-yl 2-(6-methoxynaphthalen-2-yl)propanoate (224.7 mg, 0.600 mmol, 1 equiv.), Ir(dF-ppy)₃ (4.3 mg, 0.006 mmol, 0.01 equiv.), phenol (290.5 mg, 3.00 mmol, 5 equiv.), catalytic triethylamine trihydrofluoride (30.0 μ L, 0.183 mmol, 0.1

equiv.), and DCM (3.00 mL, 0.2 M). Purified over silica with flash chromatography (2% ether in hexanes) followed by preparatory TLC (5% ether in hexanes) to afford the title compound as a clear oil (66.8 mg, 0.36 mmol, 60%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.75 (d, *J* = 1.7 Hz, 1H), 7.72 (t, *J* = 8.9 Hz, 2H), 7.49 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.22 – 7.18 (m, 2H), 7.15 (dd, *J* = 8.8, 2.6 Hz, 1H), 7.12 (d, *J* = 2.5 Hz, 1H), 6.92 (dd, *J* = 8.9, 1.1 Hz, 2H), 6.87 (tt, *J* = 7.3, 1.1 Hz, 1H), 5.45 (q, *J* = 6.4 Hz, 1H), 3.91 (s, 3H), 1.71 (d, *J* = 6.5 Hz, 3H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 158.15, 157.76, 138.56, 134.11, 129.50, 129.43, 128.89, 127.47, 124.35, 120.75, 119.09, 116.12, 105.78, 76.19, 55.45, 24.67.

HRMS: (EI-TOF) calculated for C₁₉H₁₈O₂⁺ ([M]⁺): 278.13013, found 278.12997.

FTIR (thin film, cm⁻¹): 2978 (w), 2929 (w), 2360 (w), 2342 (w), 2249 (w), 1634 (w), 1607 (m), 1598 (m), 1586 (w), 1506 (w), 1484 (s), 1464 (w), 1417 (w), 1390 (w), 1373 (w), 1303 (w), 1265 (m), 1234 (s), 1195 (m), 1170 (s), 1123 (w), 1081 (m), 1068 (m), 1028 (m), 963 (w), 905 (s), 852 (m), 811 (w), 752 (m), 727 (s), 690 (s), 675 (w), 649 (w), 551 (w), 509 (w), 475 (m), 455 (w), 420 (w).

2-methoxy-6-(1-methoxyethyl)naphthalene (47)

Synthesized according to general procedure E with minor alteration, with 1,3-dioxoisindolin-2-yl 2-(6-methoxynaphthalen-2-yl)propanoate (227.4 mg, 0.606 mmol, 1 equiv.), Ir(dF-ppy)₃ (1.7 mg, 0.0022 mmol, 0.0037 equiv.), methanol (150 μ L, 3.70 mmol, 6.1 equiv.), catalytic triethylamine trihydrofluoride (5.0 μ L, 0.031 mmol, 0.05 equiv.), and DCM (3.00 mL, 0.2 M). The anhydrous, sparged methanol was added following evacuation and backfill with nitrogen. Purified over silica with flash chromatography (7-15% EtOAc in hexanes) to afford the title compound as a white solid (0.1074 g, 0.497 mmol, 81%).

¹H NMR (500 MHz, Chloroform-*d*): δ 7.74 (t, *J* = 8.8 Hz, 2H), 7.67 (d, *J* = 1.6 Hz, 1H), 7.44 (dt, *J* = 8.5, 1.5 Hz, 1H), 7.19 – 7.13 (m, 2H), 4.43 (q, *J* = 6.5 Hz, 1H), 3.93 (s, 3H), 3.25 (s, 3H), 1.51 (d, *J* = 6.4 Hz, 3H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 157.74, 138.72, 134.28, 129.43, 128.84, 127.33, 125.22, 124.83, 119.01, 105.84, 79.85, 56.58, 55.46, 23.98.

HRMS: (EI-TOF) calculated for C₁₄H₁₆O₂⁺ [M]⁺: 216.11448, found 216.11442.

FTIR (thin film, cm⁻¹): ν 2975 (m), 2933 (m), 2855 (w), 2819 (w), 1628 (w), 1602 (m), 1504 (w), 1481 (m), 1462 (m), 1435 (m), 1416 (w), 1390 (m), 1369 (m), 1306 (m), 1263 (m), 1233 (m), 1198 (m), 1172 (s), 1161 (s), 1109 (s), 1088 (s), 1058 (s), 1026 (s), 990 (m), 960 (w), 925 (w), 890 (m), 855 (s), 816 (s), 763 (w), 750 (m), 674 (m), 620 (w), 539 (m), 524 (w), 478 (s), 470 (s), 416 (w).

2-(1-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)ethyl)-6-methoxynaphthalene (48)

Synthesized according to general procedure D with minor alteration, with 1,3-dioxoisindolin-2-yl 2-(6-methoxynaphthalen-2-yl)propanoate (75.4 mg, 0.201 mmol, 1 equiv.), Ir(dF-ppy)₃ (1.6 mg, 0.0022 mmol, 0.01 equiv.), HFIP (105 μ L, 1.00 mmol, 5 equiv.), and DCM (1.00 mL, 0.2 M). After irradiating for 24 h, 1-Fluoronaphthalene (26.0 μ L, 0.200 mmol, 1 equiv.) was added and an aliquot was analyzed by ¹⁹F-NMR to afford 66% yield (0.133 mmol, 46.7 mg). Purified over silica with flash chromatography (0-10% Et₂O in hexanes) to afford the title compound as a white solid.

¹H NMR (500 MHz, Chloroform-*d*): δ 7.79 (d, *J* = 8.5 Hz, 1H), 7.75 (d, *J* = 8.9 Hz, 1H), 7.67 (d, *J* = 1.7 Hz, 1H), 7.46 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.22 – 7.12 (m, 2H), 4.97 (q, *J* = 6.4 Hz, 1H), 4.02 (hept, *J* = 5.7 Hz, 1H), 3.94 (s, 3H), 1.66 (d, *J* = 6.5 Hz, 3H).

¹³C NMR (126 MHz, Chloroform-*d*): δ 158.42, 135.04, 134.44, 129.62, 128.50, 127.97, 127.12, 124.81, 122.42 (qq, *J* = 285.1, 2.0 Hz), 121.29 (qq, *J* = 282.5, 2.8 Hz), 119.54, 105.91, 81.67, 72.74 (hept, *J* = 32.1 Hz), 55.47, 23.18.

¹⁹F NMR (282 MHz, Chloroform-*d*): δ -72.79 (qd, *J* = 9.2, 5.7 Hz, 3F), -73.64 (qd, *J* = 9.2, 5.6 Hz, 3F).

HRMS: (EI-TOF) calculated for C₁₆H₁₄FO₂⁺ [(M*)]⁺: 352.08925 found 352.08959.

VII. Radiochemistry

General procedure and Information:

Anhydrous acetonitrile was obtained from Aldrich. [^{18}O]- H_2O was obtained from Medical Isotopes Inc. Phthalimide esters were synthesized and then stored in a $-20\text{ }^\circ\text{C}$ fridge. [^{18}F]Fluoride was produced on a General Electric (GE) 800 series PETTrace cyclotron by the nuclear reaction $^{18}\text{O}(p,n)^{18}\text{F}$ with a $65\text{ }\mu\text{A}$ beam for 5 minutes producing $\sim 300\text{ mCi}$. [^{18}F]fluoride in [^{18}O]water was pushed from the cyclotron target by hydrogen as a 2.3 mL bolus and delivered to a GE Tracerlab FX2 N synthesis module. The [^{18}F]fluoride was trapped on a Sep-Pak QMA Plus Light cartridge preconditioned with 5.0 mL of H_2O , 5 mL of 8.4% sodium bicarbonate, 5 mL of acetonitrile, and then dried with a stream of compressed air. The [^{18}F] F^- was eluted from the QMA cartridge using a 0.1 mL of potassium carbonate solution (30 mg/mL , 3 mg , 0.022 mmol in H_2O) and $4,7,13,21,24\text{-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane}$ (10 mg , 0.027 mmol) in 1.5 mL of MeCN. The resulting [^{18}F] $\text{F}^-/\text{K}_{222}/\text{K}_2\text{CO}_3$ solution was azeotropically dried and then cooled, taken up in 5 mL of MeCN, and transferred to a 10 mL septa capped scintillation vial. The vial was transferred to a separate hot cell and the [^{18}F] $\text{F}^-/\text{K}_{222}/\text{K}_2\text{CO}_3$ solution was taken up in a syringe and transferred in 0.3 or 0.5 mL aliquots to N_2 -filled, 1-dram , septa-capped vials (approx. 3 minutes with N_2 using a low flow rate of approx. 0.3 mL/min , with an 18g vent needle) precharged with photocatalyst and phthalimide ester ($0.787\text{ }\mu\text{mol}$ photocatalyst and $5.3\text{ }\mu\text{mol}$ of phthalimide ester per reaction vial) in 0.2 mL or 0.4 mL of MeCN, in the photochemistry apparatus. This typically charged the vials with $10\text{-}20\text{ mCi}$ of activity. After the addition of [^{18}F] F^- in MeCN, the vials were irradiated from the bottom for 10 minutes. *Note:* no stirring was conducted during irradiation. Following irradiation, the amount of activity present in the vial was determined by a Capintec dose calibrator. A $100\text{ }\mu\text{L}$ aliquot was taken for HPLC analysis. A $100\text{ }\mu\text{L}$ aliquot was added to a vial containing authentic ^{19}F -product for co-injection and verification of product identity via HPLC. Finally, a $100\text{ }\mu\text{L}$ aliquot was taken and diluted in 1 mL of MeCN and this solution was spotted on a silica TLC plate. The TLC plate was developed with 50% EtOAc/hexanes eluent, and then analyzed using an Eckert & Ziegler AR-2000 Radio-TLC imaging scanner to determine the radiochemical conversion.

Figure S14. Photocatalytic Radiochemical Fluorination Setup and Apparatus.

Top left: Photocatalysis set up incorporating a Kessil H150 Blue. Top middle: scintillation vial and tungsten pig used for transfer between hot cells. Top right: automated Hamilton syringe used to dispense [^{18}F]F $^-$ in MeCN solution to sparged vials. Bottom: shielding used during manual manipulations.

Figure S15. GE Tracerlab FX2 N Flow Diagram.

Teflon line to scintillation vial from VX2.

As toxic solvents and reagents present a potential translational challenge to the implementation of methodologies for [^{18}F]F $^-$ incorporation, the methylene chloride (DCM) solvent that this system was initially optimized upon was an obstacle for translation. Therefore, to enable translation, we elected to utilize acetonitrile (MeCN). In making this specific solvent change, we observed that there was a significant solvent/photocatalyst interaction effect (Table S17).

Table S17. Photocatalyst screen in MeCN.

Entry	Photocatalyst	^{19}F -NMR Yield (%) ^{a,b}
1	$\text{Ir}(\text{dF-ppy})_3$	75%
2	$\text{Ir}(\text{CF}_3\text{-ppy})_3$	89%
3	$\text{Ir}(\text{F-ppy})_3$	98%
4	$\text{Ir}(\text{ppy})_3$	64%
5	$\text{Ir}(\text{dF-tBu-ppy})_3$	83%
6	$[\text{Ir}(\text{ppy})_2(\text{dtbpy})](\text{PF}_6)$	74%
7	$[\text{Ir}(\text{dF-CF}_3\text{-ppy})_2(\text{dtbpy})](\text{PF}_6)$	71%
8	$\text{Ru}(\text{bpy})_3(\text{PF}_6)_2$	1%

^a 0.2 mmol scale reaction conducted according to general procedure D.

^b ^{19}F -NMR yields determined relative to external 1-fluoronaphthalene.

Homoleptic iridium photocatalyst were screened for the radiofluorination as previous reports have observed lowered of specific activity in radiochemical reactions when catalysts with fluoride containing counterions were utilized^{28,29} (e.g. PF₆⁻, BF₄⁻).

Table S18. Determination of Optimal Radiochemical Photocatalyst.

Photocatalyst	Run 1 EOS Activity (mCi)	Run 1 HPLC RCC (%)	Run 1 TLC RCC (%)	Run 2 EOS Activity (mCi)	Run 2 HPLC RCC (%)	Run 2 TLC RCC (%)	Average HPLC RCC (%)	Average TLC RCC (%)
Ir(F-ppy) ₃	3.94	64	58	9.92	39	45	52	51
Ir(dF-ppy) ₃	12.43	11	6	12.61	10	6	11	6
Ir(CF ₃ -ppy) ₃	12.72	28	33	8.90	41	53	35	43
Ir(dF-tBu-ppy) ₃	11.01	25	25	8.89	24	23	25	24
Ir(F-tBu-ppy) ₃	12.13	41	45	7.48	45	53	43	49

Table S19. Additive Screening for KF Solubility.

Entry	Fluoride Solubilizing Additive	¹⁹ F-NMR Yield (%) ^{a,b}
1	18-crown-6 (0.1 equiv.), CSA ^c (0.2 equiv.)	3
2	dibenzo-18-crown-6 (0.1 equiv.), CSA ^c (0.2 equiv.)	0
3	Kryptofix 2.2.2 (0.1 equiv.), CSA ^c (0.2 equiv.)	7
4	HFIP (2 equiv.)	74
5	HFIP (0.3 equiv.)	12
6	no KF	0
7	no HFIP	0

^a 0.2 mmol scale reactions conducted according to general procedure D.

^b ¹⁹F-NMR Yields determined relative to external 1-fluoronaphthalene and relative to limiting fluoride reagent.

^c CSA: camphor sulfonic acid

Based off of our previous studies conducted using 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) to produced soluble HF-species²⁸ and Table S18, we initially explored using HFIP and camphor sulfonic acid as acidic, solubilizing additives. Adding HFIP prior to sparging, we found that HFIP was not necessary for reactivity and appeared to hinder radiochemical incorporation (Table S19 and Figure S16).

Table S20. Variable Loading of HFIP as an Additive in Radiochemistry.

HFIP Additive (μL)	Run 1 EOS Activity (mCi)	Run 1 HPLC RCC (%)	Run 1 TLC RCC (%)	Run 2 EOS Activity (mCi)	Run 2 HPLC RCC (%)	Run 2 TLC RCC (%)	Average HPLC RCC (%)	Average TLC RCC (%)
0	7.83	64	60	5.62	56	67	60	60
25	5.32	42	49	5.56	38	31	40	40
50	10.37	41	31	5.35	40	37	41	34
75	1.20	42	42	4.40	43	37	43	40
100	5.93	34	32	4.19	40	33	37	33
200	8.11	27	19	4.37	29	21	28	20

Figure S16. Average RCC for Variable Loading of HFIP Additive.

Probing the photocatalyst loading on the radiochemical transformation showed an optimal loading between 8 and 16 mol% relative to phthalimide ester starting material. (A1EF5-034)

Table S21. Determining Optimal Radiochemical Photocatalyst Loading.

Photocatalyst Loading (%)	Run 1 EOS Activity (mCi)	Run 1 HPLC RCC (%)	Run 1 TLC RCC (%)	Run 2 EOS Activity (mCi)	Run 2 HPLC RCC (%)	Run 2 TLC RCC (%)	Average HPLC RCC (%)	Average TLC RCC (%)
0	5.55	0	0	9.42	0	0	0	0
2	15.66	16	12	8.59	23	34	20	23
4	13.23	25	38	7.01	28	36	27	37
8	10.11	32	51	6.83	33	33	33	42
16	12.96	28	33	6.59	39	40	34	36
32	0.42	38	30	5.56	40	30	39	30

Table S22. Concentration Evaluation.

Total volume (μ L)	Concentration (mM)	Run 1 EOS Activity (mCi)	Run 1 HPLC RCC (%)	Run 1 TLC RCC (%)
500	10.7	9.87	53	58
700	7.61	11.04	45	48
100	5.33	11.88	45	52
1200	4.44	10.24	34	54
1500	3.55	10.42	34	52
2000	2.66	9.33	32	52

Table S23. Time of Radiochemical Reaction Evaluation.

Irradiation Time (min)	Run 1		
	EOS Activity (mCi)	HPLC RCC (%)	TLC RCC (%)
0	7.19	0	0
2	7.56	48	62
5	6.15	49	71
10	10.37	45	48
15	6.65	51	67
20	5.94	48	61
30	3.79	45	64

Determination of Molar Activity and Scale Up.

To determine the molar activity of [¹⁸F]F⁻ incorporation, a UV-calibration curve was developed by serial dilution of a known quantity of [¹⁹F]-2-(1-fluoroethyl)-6-methoxynaphthalene an injection onto an Agilent 1200 series HPLC equipped with a UV- and a Lab-Logic Posi-RAM detector.

Determination of number of moles of [¹⁸F/¹⁹F]-2-(1-fluoroethyl)-6-methoxynaphthalene by Beer's Law:

$$Absorbance = \epsilon lc$$

Eq. S6

ϵ = molar absorptivity

l = path length

c = concentration

For a constant injection volume, pathlength, and molar absorptivity:

$$Absorbance \propto AX$$

Eq. S7

wherein:

X is the number of nanomoles and A is a constant

Utilizing the calibration curve, the constant A may be determined and then used to determine the quantity of [¹⁸F/¹⁹F]-2-(1-fluoroethyl)-6-methoxynaphthalene.

Table S24. Molar Activity Calibration Curve.

Dilution	Final Concentration (10 ⁻⁵ M)	Moles Injected (10 ⁻⁹ mol)	Absorbance Area 1 (mAu)	Absorbance Area 2 (mAu)	Avg. Absorbance Area (mAu)
1.3 mg 1 in 10.00 mL (Sol 1)	63.7	15.9	3254.1	3316.1	3285.1
1000 μ L Sol 1 to 5.00 mL	12.7	3.18	667.2	661.3	664.25
700 μ L Sol 1 to 5.00 mL	8.91	2.23	460.6	463.0	461.8
400 μ L Sol 1 to 5.00 mL	5.09	1.27	263.9	265.5	264.7
100 μ L Sol 1 to 5.00 mL	1.27	0.318	64.5	66.2	65.4
100 μ L Sol 1 to 50.00 mL	0.127	0.0318	5.4	5.6	5.5
Slope (mAu/nmol):					206.6
Std. Dev. Slope (mAu/nmol):					0.21
R ² :					1.00

Figure S17. Molar Activity Calibration Curve.

Following the determination of a specific activity curve, scale ups using higher activity (50-100 mCi) were conducted. The [¹⁸F]-2-(1-fluoroethyl)-6-methoxynaphthalene peak was isolated from the HPLC and the isolated activity was determined as well as the absorbance of the peak. From this the specific activity was determined by dividing the activity by the amount of fluorinated product.

$$Absorbance = AX$$

$$\frac{Absorbance}{A} = \frac{Absorbance}{206.6 \frac{mAu}{nmol}} = X \text{ nmol}$$

Eq. S8

$$Specific \text{ Activity} = \frac{Activity}{X \text{ nmol}}$$

Eq. S9

Table S25. Molar Activity Determination.

Entry	Activity (mCi, EOS)	Isolated Rad. (μ Ci)	Isolated Absorbance (mAu)	HPLC RCC (%)	Specific Activity (mCi/nmol, EOS)
1	103.2	205	62.4	22	1.56
2	79.7	156	158.9	17	0.590
3	65.2	87	80.9	21	0.815
Average Molar Activity (mCi/nmol):					0.99
Std. Dev. Molar Activity (mCi/nmol):					0.51

Evaluation of Radiochemical Scope

2-(1-(fluoro-¹⁸F)ethyl)-6-methoxynaphthalene ([¹⁸F]2)

A vial was charged with 1,3-dioxoisindolin-2-yl 2-(6-methoxynaphthalen-2-yl)propanoate (14.5 mg, 0.0386 mmol, 1 equiv.) and 4.44 mg of Ir(F-ppy)₃ (4.44 mg, 0.00582 mmol, 0.15 equiv.) MeCN (2.8 mL) was added to the vial and used to dissolve all of the solids. Aliquots (400 μ L) were then removed from the vial and added to 5 separate vials. These vials were septa capped and subjected to the general procedure for radiochemistry. 2-(1-(fluoro-¹⁸F)ethyl)-6-methoxynaphthalene was determined to be obtained by coinjection with authentic 2-(1-(fluoro-¹⁹F)ethyl)-6-methoxynaphthalene. This procedure was repeated to furnish additional replicates.

Table S26. Replicates for generation of 2-(1-(fluoro-¹⁸F)ethyl)-6-methoxynaphthalene.

Entry	Activity at EOS (mCi)	RCC-TLC (%, 50% EtOAc in hexanes)	RCC-HPLC (%)
1	13.14	61	63
2	16.63	49	36
3	16.10	47	31
4	13.61	44	29
5	11.71	44	34
6	103.2	11	22
7	79.7	13	17
8	65.2	10	21

Figure S18. HPLC of Authentic Standards at 254 nm (**1**, **2**, and Ir(F-ppy)₃).

HPLC Column: Zorbax SB-C18, 5 μ m, 4.6x250 mm. 2-(1-(fluoro-¹⁹F)ethyl)-6-methoxynaphthalene (**2**), 8:44 min. 1,3-dioxoisindolin-2-yl 2-(6-methoxynaphthalen-2-yl)propanoate (**1**), 11:01 min. Ir(F-ppy)₃, 19:55 min.

Figure S19. PosiRam-HPLC of Crude Reaction Mixture with 2-(1-(fluoro-¹⁸F)ethyl)-6-methoxynaphthalene ([¹⁸F]**2**).

Figure S20. HPLC of Crude Reaction Mixture with 2-(1-(fluoro- ^{18}F)ethyl)-6-methoxynaphthalene (^{18}F **2**) at 254 nm.

Figure S21. HPLC of Crude Reaction Mixture with 2-(1-(fluoro- ^{18}F)ethyl)-6-methoxynaphthalene (^{18}F **2**) with Coinjection (**2**).

Figure S22. Sample Radio-TLC of 2-(1-(fluoro- ^{18}F)ethyl)-6-methoxynaphthalene (^{18}F **2**). Region 1: Inorganic (“free” and unincorporated) ^{18}F F $^-$ at baseline of plate; Region 2: 2-(1-(fluoro- ^{18}F)ethyl)-6-methoxynaphthalene (^{18}F **2**).

Figure S23. Sample Radio-TLC of the $[^{18}\text{F}]\text{F}^-/\text{K}_{222}/\text{K}_2\text{CO}_3$ (unincorporated $[^{18}\text{F}]\text{F}^-$, 50% EtOAc/hexanes eluent).

2-(1-(fluoro- ^{18}F)ethyl)-6-methoxynaphthalene ([^{18}F]30)

A vial was charged with 1,3-dioxoisindolin-2-yl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (30.5 mg, 0.0800 mmol, 1 equiv.) and 3.0 mL of MeCN. The solid was dissolved and 200 μL aliquots was added to 5 separate vials. Similarly, a separate vial was charged with $\text{Ir}(\text{dF-ppy})_3$ (5.22 mg, 0.00684 mmol, 0.18 equiv.). MeCN (1.400 mL) was added to the vial and used to suspend the photocatalyst. Aliquots of 200 μL of photocatalyst solution and of phthalimide ester solution were then added to separate vials to have vials with 400 μL of photocatalyst and phthalimide ester. The vials were septa capped and subjected to the general procedure for radiochemistry. This procedure was repeated to furnish additional replicates.

Note: we found $\text{Ir}(\text{F-ppy})_3$ was less effective for this substrate under radiochemical conditions.

Table S27. Replicates for Generation of 2-((4-(fluoro-¹⁸F)-4-methylpentyl)oxy)-1,4-dimethylbenzene ([¹⁸F]**30**).

Entry	Activity at EOS (mCi)	RCC-TLC (% 50% EtOAc in hexanes)	RCC-HPLC (%)
1	14.50	10	15
2	9.84	10	14
3	6.05	7	17
4	3.83	11	14
5	5.75	6	16

Figure S24. HPLC of Authentic Materials: 2-((4-fluoro-4-methylpentyl)oxy)-1,4-dimethylbenzene (**30**, 7:08 min) and 1,3-dioxoisindolin-2-yl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (**41**, 8:45 min) at 254 nm.

Figure S25. HPLC of Authentic Ir(dF-ppy)₃ (14.33 min) at 254 nm.

Figure S26. Sample HPLC of Crude Reaction Mixture with 2-((4-(fluoro- ^{18}F)-4-methylpentyl)oxy)-1,4-dimethylbenzene ($[\text{}^{18}\text{F}]\text{30}$, Posi-RAM).

Figure S27. Sample HPLC of Crude 2-((4-(fluoro- ^{18}F)-4-methylpentyl)oxy)-1,4-dimethylbenzene ($[\text{}^{18}\text{F}]\text{30}$, 254 nm).

Figure S28. Sample HPLC of Crude 2-((4-(fluoro- ^{18}F)-4-methylpentyl)oxy)-1,4-dimethylbenzene ($[\text{}^{18}\text{F}]\text{30}$) with 2-((4-fluoro-4-methylpentyl)oxy)-1,4-dimethylbenzene (**30**) Coinjection (254 nm).

Figure S29. Sample Radio-TLC of 2-((4-(fluoro- ^{18}F)-4-methylpentyl)oxy)-1,4-dimethylbenzene (^{18}F 2). Region 1: Inorganic ("free" and unincorporated) $^{18}\text{F}^-$ at baseline of plate; Region 2: 2-((4-(fluoro- ^{18}F)-4-methylpentyl)oxy)-1,4-dimethylbenzene (^{18}F 30).

Reg	(mm) Start	(mm) Stop	(mm) Centroid	RF	Region Counts	Region CPM	% of Total	% of ROI
Rgn 1	1.9	30.2	14.7	0.147	214150.0	71383.3	86.39	89.26
Rgn 2	67.1	89.5	79.0	0.790	25772.0	8590.7	10.40	10.74
2 Peaks					239922.0	79974.0	96.79	100.00

(3aR,4R,6R,6aS)-4-(benzyloxy)-6-(fluoro- ^{18}F)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxole (^{18}F 34)

A vial was charged with 1,3-dioxoisindolin-2-yl (3a*S*,4*S*,6*R*,6a*R*)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxole-4-carboxylate (35.1 mg, 0.0800 mmol, 1 equiv.) and 3.0 mL of MeCN. The solid was dissolved and 200 μL aliquots was added to 5 separate vials. Similarly, a separate vial was charged with 5.03 mg of $\text{Ir}(\text{F-ppy})_3$ (5.03 mg, 0.00710 mmol, 0.19 mmol). MeCN (1.400 mL) was added to the vial and used to suspend the photocatalyst. Aliquots of 200 μL of photocatalyst solution and of phthalimide ester solution were then added to separate vials to have vials with 400 μL of photocatalyst and phthalimide ester. The vials were septa capped and then subjected to the general procedure for radiochemistry. (3a*R*,4*R*,6*R*,6a*S*)-4-(benzyloxy)-6-(fluoro- ^{18}F)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxole was determined to be obtained by co-spotting in the course of radio TLC with authentic (3a*R*,4*R*,6*R*,6a*S*)-4-(benzyloxy)-6-(fluoro- ^{18}F)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxole. This procedure was repeated to furnish additional replicates.

Note: This substrate appeared to undergo decomposition (likely acetal deprotection) under HPLC conditions thereby prohibiting identity confirmation by HPLC coinjection.

Table S28. Replicates for Generation of (3a*R*,4*R*,6*R*,6a*S*)-4-(benzyloxy)-6-(fluoro-¹⁸F)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxole ([¹⁸F]**34**).

Entry	Activity at EOS (mCi)	RCC-TLC (%, 50% EtOAc in hexanes)
1	1.41	65
2	11.16	25
3	4.79	39
4	4.74	33
5	2.25	49

Figure S30. Sample Radio-TLC of 2-((4-(fluoro-¹⁸F)-4-methylpentyl)oxy)-1,4-dimethylbenzene ([¹⁸F]**34**). Region 1: Inorganic (“free” and unincorporated) [¹⁸F]F⁻ at baseline of plate; Region 2: (3a*R*,4*R*,6*R*,6a*S*)-4-(benzyloxy)-6-(fluoro-¹⁸F)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxole ([¹⁸F]**34**).

Reg	(mm) Start	(mm) Stop	(mm) Centroid	RF	Region Counts	Region CPM	% of Total	% of ROI
Rgn 1	4.5	21.6	13.0	0.130	103756.0	34585.3	43.57	51.81
Rgn 2	56.8	79.2	65.2	0.652	96508.0	32169.3	40.53	48.19
2 Peaks					200264.0	66754.7	84.10	100.00

VIII. NMR Spectra

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl 2-(6-methoxynaphthalen-2-yl)propanoate (**1**) in CDCl_3

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl 2-(6-methoxynaphthalen-2-yl)propanoate (**1**) in CDCl_3

500 MHz ^1H -NMR of 4,5,6,7-tetrachloro-1,3-dioxoisindolin-2-yl 2-(6-methoxynaphthalen-2-yl)propanoate (**S1**) in CDCl_3

126 MHz ^{13}C -NMR of 4,5,6,7-tetrachloro-1,3-dioxoisindolin-2-yl 2-(6-methoxynaphthalen-2-yl)propanoate (**S1**) in CDCl_3

500 MHz ^1H -NMR of 2-(1-fluoroethyl)-6-methoxynaphthalene (**2**) in CDCl_3

126 MHz ^{13}C -NMR of 2-(1-fluoroethyl)-6-methoxynaphthalene (**2**) in CDCl_3

376 MHz ^{19}F -NMR of 2-(1-fluoroethyl)-6-methoxynaphthalene (**2**) in CDCl_3

[illegible]

Chemical structure: CC(C)(C)c1ccc(cc1)C(=O)O

¹³C NMR spectrum (ppm):

- 168.00
- 162.04
- 150.85
- 134.94
- 129.08
- 129.06
- 128.68
- 125.98
- 124.15
- 37.31
- 34.70
- 31.46

500 MHz ^1H -NMR of 1-(*tert*-butyl)-4-(fluoromethyl)benzene (**7**) in CDCl_3

126 MHz ^{13}C -NMR of 1-(*tert*-butyl)-4-(fluoromethyl)benzene (**7**) in CDCl_3

282 MHz ^{19}F -NMR of 1-(*tert*-butyl)-4-(fluoromethyl)benzene (**7**) in CDCl_3

400 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl 2-([1,1'-biphenyl]-4-yl)acetate (**S3**) in CDCl_3

101 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl 2-([1,1'-biphenyl]-4-yl)acetate (**S3**) in CDCl_3

500 MHz ^1H -NMR of 4-(fluoromethyl)-1,1'-biphenyl (**8**) in CDCl_3

126 MHz ^{13}C -NMR of 4-(fluoromethyl)-1,1'-biphenyl (**8**) in CDCl_3

376 MHz ^{19}F -NMR of 4-(fluoromethyl)-1,1'-biphenyl (**8**) in CDCl_3

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl 2-(4-iodophenyl)acetate (**S4**) in CDCl_3

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl 2-(4-iodophenyl)acetate (**S4**) in CDCl_3

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl 2-(4-(benzyloxy)phenyl)acetate (**S5**) in CD_2Cl_2

126 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl 2-(4-(benzyloxy)phenyl)acetate (**S5**) in CD_2Cl_2

500 MHz ^1H -NMR of 1-(benzyloxy)-4-(fluoromethyl)benzene (**10**) in CDCl_3

126 MHz ^{13}C -NMR of 1-(benzyloxy)-4-(fluoromethyl)benzene (**10**) in CDCl_3

282 MHz ^{19}F -NMR of 1-(benzyloxy)-4-(fluoromethyl)benzene (**10**) in CDCl_3

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl 2-(4-(methylthio)phenyl)acetate (**S6**) in CD_2Cl_2

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl 2-(4-(methylthio)phenyl)acetate (**S6**) in CD_2Cl_2

500 MHz ^1H -NMR of (4-(fluoromethyl)phenyl)(methyl)sulfane (**11**) in CD_2Cl_2

Chemical structure: COc1ccc(CF)cc1

¹³C NMR spectrum (ppm):

- 140.34
- 139.19
- 138.13
- 133.23
- 129.54
- 128.95
- 127.87
- 126.66
- 85.60
- 84.29
- 54.00 CDCl₃
- 37.87
- 16.39
- 15.82

Cc1ccc(CF)cc1

Chemical structure of 4-fluorobenzyl methyl sulfide (4-FBMS) is shown. The structure consists of a benzene ring with a methyl sulfide group (-SMe) at the para position and a fluoromethyl group (-CH₂F) at the other para position.

The ¹⁹F NMR spectrum shows a triplet signal centered around -204.4 ppm, characteristic of the -CH₂F group. The chemical shift values are labeled as -204.22, -204.39, and -204.56 ppm. The integration value for this signal is 1.00.

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl 2-(4-acetamidophenyl)acetate (**S7**) in CDCl_3

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl 2-(4-acetamidophenyl)acetate (**S7**) in CDCl_3

500 MHz ^1H -NMR of *N*-(4-(fluoromethyl)phenyl)acetamide (**12**) in CDCl_3

126 MHz ^{13}C -NMR of *N*-(4-(fluoromethyl)phenyl)acetamide (**12**) in CDCl_3

376 MHz ^{19}F -NMR of *N*-(4-(fluoromethyl)phenyl)acetamide (**12**) in CDCl_3

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl 2-(4-(trifluoromethoxy)phenyl)acetate (**S8**) in CDCl_3

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl 2-(4-(trifluoromethoxy)phenyl)acetate (**S8**) in CDCl_3

282 MHz ^{19}F -NMR of 1,3-dioxoisindolin-2-yl 2-(4-(trifluoromethoxy)phenyl)acetate (**S8**) in CDCl_3

282 MHz ^{19}F -NMR of 1-(fluoromethyl)-4-(trifluoromethoxy)benzene (**13**) in CDCl_3

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl 2-(4-(trifluoromethyl)phenyl)acetate (**S9**) in CDCl_3

Chemical structure: FC(F)(F)c1ccc(cc1)CC(=O)Oc2c(=O)c3ccccc3n2

¹³C NMR spectrum (CDCl₃) showing peaks at the following chemical shifts (ppm):

- 167.18
- 161.88
- 156.88
- 135.59
- 135.58
- 135.57
- 135.05
- 130.74
- 130.48
- 130.22
- 129.96
- 129.88
- 129.86
- 129.85
- 126.03
- 126.00
- 125.97
- 125.94
- 125.20
- 124.22
- 123.03
- 120.87
- 77.16 CDCl₃
- 37.60

Chemical structure of the compound is shown above the spectrum. The spectrum displays a single sharp peak at $\delta = 62.67$ ppm, corresponding to the carbonyl carbon of the phthalimide group. The integration value for this peak is 3.00.

282 MHz ^{19}F -NMR of 1-(fluoromethyl)-4-(trifluoromethyl)benzene (**14**) in CDCl_3

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl 2-(benzo[d][1,3]dioxol-5-yl)acetate (**S10**) in CDCl_3

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl 2-(benzo[d][1,3]dioxol-5-yl)acetate (**S10**) in CDCl_3

500 MHz ^1H -NMR of 5-(fluoromethyl)benzo[d][1,3]dioxole (**15**) in CD_2Cl_2

126 MHz ^{13}C -NMR of 5-(fluoromethyl)benzo[*d*][1,3]dioxole (**15**) in CD_2Cl_2

376 MHz ^{19}F -NMR of 5-(fluoromethyl)benzo[*d*][1,3]dioxole (**15**) in CD_2Cl_2

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl 2-(4-bromothiophen-2-yl)acetate (**S11**) in CDCl_3

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl 2-(4-bromothiophen-2-yl)acetate (**S11**) in CDCl_3

282 MHz ^{19}F -NMR of 4-bromo-2-(fluoromethyl)thiophene (**16**) in CDCl_3

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl 2-cyclopentyl-2-(4-(trifluoromethyl)phenyl)acetate (**S12**) in CDCl_3

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl 2-cyclopentyl-2-(4-(trifluoromethyl)phenyl)acetate (**S12**) in CDCl_3

282 MHz ^{19}F -NMR of 1,3-dioxoisindolin-2-yl 2-cyclopentyl-2-(4-(trifluoromethyl)phenyl)acetate (**S12**) in CDCl_3

500 MHz ^1H -NMR of 1-(cyclopentylfluoromethyl)-4-(trifluoromethyl)benzene (**17**) in CDCl_3

126 MHz ^{13}C -NMR of 1-(cyclopentylfluoromethyl)-4-(trifluoromethyl)benzene (**17**) in CDCl_3

376 MHz ^{19}F -NMR of 1-(cyclopentylfluoromethyl)-4-(trifluoromethyl)benzene (**17**) in CDCl_3

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl 2-(6-chloropyridin-3-yl)propanoate (**S13**) in CD_2Cl_2

126 MHz ^{13}C -NMR of 1,3-dioxisoindolin-2-yl 2-(6-chloropyridin-3-yl)propanoate (**S13**) in CD_2Cl_2

500 MHz ^1H -NMR of 2-chloro-5-(1-fluoroethyl)pyridine (**18**) in CD_2Cl_2

126 MHz ^{13}C -NMR of 2-chloro-5-(1-fluoroethyl)pyridine (**18**) in CD_2Cl_2

282 MHz ^{19}F -NMR of 2-chloro-5-(1-fluoroethyl)pyridine (**18**) in CD_2Cl_2

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl 4-(dimethylamino)-2-(naphthalen-2-yl)-4-oxobutanoate (**S15**) in CDCl_3

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl 4-(dimethylamino)-2-(naphthalen-2-yl)-4-oxobutanoate (**S14**) in CDCl_3

500 MHz ^1H -NMR of ($\pm$)-3-fluoro-*N,N*-dimethyl-3-(naphthalen-2-yl)propenamide (**19**) in CDCl_3

126 MHz ^{13}C -NMR of 3-fluoro-*N,N*-dimethyl-3-(naphthalen-2-yl)propenamide (**19**) in CDCl_3

282 MHz ^{19}F -NMR of ($\pm$)-3-fluoro-*N,N*-dimethyl-3-(naphthalen-2-yl)propenamide (**19**) in CDCl_3

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl 2-(4-(azidomethyl)phenyl)propanoate (**S15**) in CDCl_3

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl 2-(4-(azidomethyl)phenyl)propanoate (**S15**) in CDCl_3

500 MHz ^1H -NMR of 1-(azidomethyl)-4-(1-fluoroethyl)benzene (**20**) in CDCl_3

126 MHz ^{13}C -NMR of 1-(azidomethyl)-4-(1-fluoroethyl)benzene (**20**) in CDCl_3

376 MHz ^{19}F -NMR of 1-(azidomethyl)-4-(1-fluoroethyl)benzene (**20**) in CDCl_3

Chemical structure: CC(=O)N1C(=O)c2ccccc21C(=O)c3ccccc3C(=O)c4ccccc4

¹H NMR spectrum (CDCl₃) showing peaks from 1.4 to 8.0 ppm. The spectrum includes aromatic signals (7.4-8.0 ppm), a methine proton (4.2 ppm), and a methyl group (1.5 ppm). Integration values are provided below the peaks.

Chemical Structure: 1-methyl-2-(2-benzoylphenyl)isoindolin-1-one

¹³C NMR Spectrum (ppm):

- 198.44
- 170.57
- 138.74
- 138.39
- 137.47
- 134.95
- 132.72
- 132.72
- 131.67
- 130.35
- 129.46
- 129.13
- 128.52
- 124.13
- 43.00
- 19.04

Inset Spectrum (ppm):

- 138.74
- 138.39
- 137.47
- 134.95
- 132.72
- 131.67
- 130.35
- 129.46
- 129.13
- 128.52
- 124.13

Chemical structure: CC(=O)c1ccccc1F

¹H NMR spectrum (CDCl₃) showing peaks from 1.5 to 8.0 ppm. Integration values are provided below the peaks: 3.01, 3.00, 3.00, 1.01, and 3.01.

Chemical structure: CC(F)[C@@H](CS)C1=CC=C(C(=O)C2=CC=CC=C2)C=C1

¹³C NMR spectrum (CDCl₃) showing peaks at the following chemical shifts (ppm):

- 198.20
- 143.09
- 141.93
- 137.90
- 137.50
- 132.74
- 130.88
- 130.62
- 129.21
- 128.65
- 128.54
- 126.78
- 61.29
- 59.59
- 23.23
- 23.03

CC(F)c1ccc(cc1)C(=O)c2ccccc2

Chemical structure of (S)-1-(4-(1-fluoroethyl)phenyl)ethan-1-one is shown. The structure consists of a benzophenone core with a 1-fluoroethyl group attached to the para position of one of the phenyl rings.

The ¹³C NMR spectrum (CDCl₃) shows the following chemical shifts (ppm):

- 168.49
- 168.47
- 168.53
- 168.55
- 168.66
- 168.72

The spectrum displays a cluster of peaks between 168.4 and 168.8 ppm, corresponding to the carbonyl and aromatic regions. A reference peak for TMS is visible at 0 ppm.

CC(C)(C(=O)Oc1ccccc1)c2ccccc2

Chemical structure: 2-(2,2-dimethyl-1-phenylpropan-1-onyl)benzoxazol-4(3H)-one

¹H NMR spectrum (CDCl₃) showing peaks in the aromatic region (7.2-7.9 ppm) and aliphatic region (1.4-1.8 ppm). Integration values are provided for the aliphatic peaks.

Chemical Shift (ppm)	Integration
7.88	1.98
7.87	2.00
7.86	1.97
7.79	1.97
7.78	1.97
7.77	0.98
7.76	
7.75	
7.51	
7.49	
7.48	
7.44	
7.42	
7.41	
7.34	
7.33	
7.32	
7.32	
7.31	
7.26	
1.79	6.00
1.55	

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl 2-methyl-2-phenylpropanoate (**S17**) in CDCl_3

500 MHz ^1H -NMR of (2-fluoropropan-2-yl)benzene (**22**) in CDCl_3

126 MHz ^{13}C -NMR of (2-fluoropropan-2-yl)benzene (**22**) in CDCl_3

282 MHz ^{19}F -NMR of (2-fluoropropan-2-yl)benzene (**22**) in CDCl_3

500 MHz ¹H-NMR of 1,3-dioxoisindolin-2-yl 1-(4-chlorophenyl)cyclohexane-1-carboxylate (**S18**) in CDCl₃ 126 MHz ¹³C-NMR of 1,3-dioxoisindolin-2-yl 1-(4-chlorophenyl)cyclohexane-1-carboxylate (**S18**) in CDCl₃

500 MHz ^1H -NMR of 1-chloro-4-(1-fluorocyclohexyl)benzene (**23**) in CDCl_3

126 MHz ^{13}C -NMR of 1-chloro-4-(1-fluorocyclohexyl)benzene (**23**) in CDCl_3

376 MHz ^{19}F -NMR of 1-chloro-4-(1-fluorocyclohexyl)benzene (**23**) in CDCl_3

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl 1-(4-chlorophenyl)cyclopentane-1-carboxylate (**S19**) in CDCl_3

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl 1-(4-chlorophenyl)cyclopentane-1-carboxylate (**S19**) in CDCl_3

470 MHz ^{19}F -NMR of 1-chloro-4-(1-fluorocyclopentyl)benzene (**24**) in CDCl_3

500 MHz ¹H-NMR of 1,3-dioxoisindolin-2-yl 1-(4-chlorophenyl)cyclobutane-1-carboxylate (**S20**) in CDCl₃

Clc1ccc(cc1)C2(CCC2)C(=O)OC(=O)c3cc4c(cc3)oc(=O)n4

13C NMR spectrum (CDCl₃) showing peaks at the following chemical shifts (ppm):

- 171.96
- 162.05
- 139.81
- 134.89
- 133.52
- 129.12
- 128.98
- 128.05
- 124.06
- 77.46 (CDCl₃)
- 50.62
- 32.82
- 16.87

Chemical structure: Clc1ccc(cc1)C2(F)CC3CC23

¹H NMR spectrum (ppm):

- 7.73, 7.72, 7.71, 7.70, 7.69, 7.68, 7.66, 7.65, 7.64, 7.59, 7.58, 7.57, 7.56, 7.55, 7.54, 7.53, 7.52, 7.51, 7.50, 7.49, 7.48, 7.47, 7.46, 7.45, 7.44, 7.43, 7.42, 7.41, 7.40, 7.39, 7.38, 7.37, 7.36, 7.35, 7.34, 7.33, 7.32, 7.31, 7.30, 7.29, 7.28, 7.27, 7.26, 7.25, 7.24, 7.23, 7.22, 7.21, 7.20, 7.19, 7.18, 7.17, 7.16, 7.15, 7.14, 7.13, 7.12, 7.11, 7.10, 7.09, 7.08, 7.07, 7.06, 7.05, 7.04, 7.03, 7.02, 7.01, 7.00, 6.99, 6.98, 6.97, 6.96, 6.95, 6.94, 6.93, 6.92, 6.91, 6.90, 6.89, 6.88, 6.87, 6.86, 6.85, 6.84, 6.83, 6.82, 6.81, 6.80, 6.79, 6.78, 6.77, 6.76, 6.75, 6.74, 6.73, 6.72, 6.71, 6.70, 6.69, 6.68, 6.67, 6.66, 6.65, 6.64, 6.63, 6.62, 6.61, 6.60, 6.59, 6.58, 6.57, 6.56, 6.55, 6.54, 6.53, 6.52, 6.51, 6.50, 6.49, 6.48, 6.47, 6.46, 6.45, 6.44, 6.43, 6.42, 6.41, 6.40, 6.39, 6.38, 6.37, 6.36, 6.35, 6.34, 6.33, 6.32, 6.31, 6.30, 6.29, 6.28, 6.27, 6.26, 6.25, 6.24, 6.23, 6.22, 6.21, 6.20, 6.19, 6.18, 6.17, 6.16, 6.15, 6.14, 6.13, 6.12, 6.11, 6.10, 6.09, 6.08, 6.07, 6.06, 6.05, 6.04, 6.03, 6.02, 6.01, 6.00, 5.99, 5.98, 5.97, 5.96, 5.95, 5.94, 5.93, 5.92, 5.91, 5.90, 5.89, 5.88, 5.87, 5.86, 5.85, 5.84, 5.83, 5.82, 5.81, 5.80, 5.79, 5.78, 5.77, 5.76, 5.75, 5.74, 5.73, 5.72, 5.71, 5.70, 5.69, 5.68, 5.67, 5.66, 5.65, 5.64, 5.63, 5.62, 5.61, 5.60, 5.59, 5.58, 5.57, 5.56, 5.55, 5.54, 5.53, 5.52, 5.51, 5.50, 5.49, 5.48, 5.47, 5.46, 5.45, 5.44, 5.43, 5.42, 5.41, 5.40, 5.39, 5.38, 5.37, 5.36, 5.35, 5.34, 5.33, 5.32, 5.31, 5.30, 5.29, 5.28, 5.27, 5.26, 5.25, 5.24, 5.23, 5.22, 5.21, 5.20, 5.19, 5.18, 5.17, 5.16, 5.15, 5.14, 5.13, 5.12, 5.11, 5.10, 5.09, 5.08, 5.07, 5.06, 5.05, 5.04, 5.03, 5.02, 5.01, 5.00, 4.99, 4.98, 4.97, 4.96, 4.95, 4.94, 4.93, 4.92, 4.91, 4.90, 4.89, 4.88, 4.87, 4.86, 4.85, 4.84, 4.83, 4.82, 4.81, 4.80, 4.79, 4.78, 4.77, 4.76, 4.75, 4.74, 4.73, 4.72, 4.71, 4.70, 4.69, 4.68, 4.67, 4.66, 4.65, 4.64, 4.63, 4.62, 4.61, 4.60, 4.59, 4.58, 4.57, 4.56, 4.55, 4.54, 4.53, 4.52, 4.51, 4.50, 4.49, 4.48, 4.47, 4.46, 4.45, 4.44, 4.43, 4.42, 4.41, 4.40, 4.39, 4.38, 4.37, 4.36, 4.35, 4.34, 4.33, 4.32, 4.31, 4.30, 4.29, 4.28, 4.27, 4.26, 4.25, 4.24, 4.23, 4.22, 4.21, 4.20, 4.19, 4.18, 4.17, 4.16, 4.15, 4.14, 4.13, 4.12, 4.11, 4.10, 4.09, 4.08, 4.07, 4.06, 4.05, 4.04, 4.03, 4.02, 4.01, 4.00, 3.99, 3.98, 3.97, 3.96, 3.95, 3.94, 3.93, 3.92, 3.91, 3.90, 3.89, 3.88, 3.87, 3.86, 3.85, 3.84, 3.83, 3.82, 3.81, 3.80, 3.79, 3.78, 3.77, 3.76, 3.75, 3.74, 3.73, 3.72, 3.71, 3.70, 3.69, 3.68, 3.67, 3.66, 3.65, 3.64, 3.63, 3.62, 3.61, 3.60, 3.59, 3.58, 3.57, 3.56, 3.55, 3.54, 3.53, 3.52, 3.51, 3.50, 3.49, 3.48, 3.47, 3.46, 3.45, 3.44, 3.43, 3.42, 3.41, 3.40, 3.39, 3.38, 3.37, 3.36, 3.35, 3.34, 3.33, 3.32, 3.31, 3.30, 3.29, 3.28, 3.27, 3.26, 3.25, 3.24, 3.23, 3.22, 3.21, 3.20, 3.19, 3.18, 3.17, 3.16, 3.15, 3.14, 3.13, 3.12, 3.11, 3.10, 3.09, 3.08, 3.07, 3.06, 3.05, 3.04, 3.03, 3.02, 3.01, 3.00, 2.99, 2.98, 2.97, 2.96, 2.95, 2.94, 2.93, 2.92, 2.91, 2.90, 2.89, 2.88, 2.87, 2.86, 2.85, 2.84, 2.83, 2.82, 2.81, 2.80, 2.79, 2.78, 2.77, 2.76, 2.75, 2.74, 2.73, 2.72, 2.71, 2.70, 2.69, 2.68, 2.67, 2.66, 2.65, 2.64, 2.63, 2.62, 2.61, 2.60, 2.59, 2.58, 2.57, 2.56, 2.55, 2.54, 2.53, 2.52, 2.51, 2.50, 2.49, 2.48, 2.47, 2.46, 2.45, 2.44, 2.43, 2.42, 2.41, 2.40, 2.39, 2.38, 2.37, 2.36, 2.35, 2.34, 2.33, 2.32, 2.31, 2.30, 2.29, 2.28, 2.27, 2.26, 2.25, 2.24, 2.23, 2.22, 2.21, 2.20, 2.19, 2.18, 2.17, 2.16, 2.15, 2.14, 2.13, 2.12, 2.11, 2.10, 2.09, 2.08, 2.07, 2.06, 2.05, 2.04, 2.03, 2.02, 2.01, 2.00, 1.99, 1.98, 1.97, 1.96, 1.95, 1.94, 1.93, 1.92, 1.91, 1.90, 1.89, 1.88, 1.87, 1.86, 1.85, 1.84, 1.83, 1.82, 1.81, 1.80, 1.79, 1.78, 1.77, 1.76, 1.75, 1.74, 1.73, 1.72, 1.71, 1.70, 1.69, 1.68, 1.67, 1.66, 1.65, 1.64, 1.63, 1.62, 1.61, 1.60, 1.59, 1.58, 1.57, 1.56, 1.55, 1.54, 1.53, 1.52, 1.51, 1.50, 1.49, 1.48, 1.47, 1.46, 1.45, 1.44, 1.43, 1.42, 1.41, 1.40, 1.39, 1.38, 1.37, 1.36, 1.35, 1.34, 1.33, 1.32, 1.31, 1.30, 1.29, 1.28, 1.27, 1.26, 1.25, 1.24, 1.23, 1.22, 1.21, 1.20,

126 MHz ^{13}C -NMR of 1-chloro-4-(1-fluorocyclobutyl)benzene (**25**) in CDCl_3

470 MHz ^{19}F -NMR of 1-chloro-4-(1-fluorocyclobutyl)benzene (**25**) in CDCl_3

400 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl 4-(6-chloropyridin-3-yl)tetrahydro-2H-pyran-4-carboxylate (**S21**) in CDCl_3

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl 4-(6-chloropyridin-3-yl)tetrahydro-2*H*-pyran-4-carboxylate (**S21**) in CDCl_3

500 MHz ^1H -NMR of 2-chloro-5-(4-fluorotetrahydro-2*H*-pyran-4-yl)pyridine (**26**) in CDCl_3

126 MHz ^{13}C -NMR of 2-chloro-5-(4-fluorotetrahydro-2H-pyran-4-yl)pyridine (**26**) in CDCl_3

282 MHz ^{19}F -NMR of 2-chloro-5-(4-fluorotetrahydro-2H-pyran-4-yl)pyridine (**26**) in CDCl_3

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl adamantane-1-carboxylate (**S22**) in CDCl_3

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl adamantane-1-carboxylate (**S22**) in CDCl_3

500 MHz ^1H -NMR of 1,3-dioxisoindolin-2-yl 3-(4-(*tert*-butyl)phenyl)-2,2-dimethylpropanoate (**S23**) in CDCl_3

126 MHz ^{13}C -NMR of 1,3-dioxisoindolin-2-yl 3-(4-(*tert*-butyl)phenyl)-2,2-dimethylpropanoate (**S23**) in CDCl_3

500 MHz ^1H -NMR of 1-(tert-butyl)-4-(2-fluoro-2-methylpropyl)benzene (**28**) in CDCl_3

126 MHz ^{13}C -NMR of 1-(tert-butyl)-4-(2-fluoro-2-methylpropyl)benzene (**28**) in CDCl_3

CC(C)(F)Cc1ccc(C(C)(C)C)cc1

Chemical structure of **1** (4-cyanobenzyl 2-methyl-1-phenylisoindol-1-one-3-carboxylate) is shown with its ¹H NMR spectrum (CDCl₃, 40 °C). The spectrum displays peaks for the compound, with chemical shifts (ppm) indicated above the peaks: 7.91, 7.90, 7.90, 7.89, 7.88, 7.82, 7.81, 7.80, 7.64, 7.63, 7.62, 7.46, and 7.44. The structure includes a nitrile group (NC) and a methyl group (Me).

Chemical structure: CN1C(=O)c2ccccc2C1(C)Cc3ccc(C#N)cc3

¹³C NMR spectrum (CDCl₃) showing peaks (ppm):

- 173.11
- 162.15
- 142.19
- 134.99
- 132.25
- 131.31
- 129.68
- 124.15
- 119.04
- 111.12
- 77.46 (CDCl₃)
- 46.03
- 43.35
- 25.28

CN#Cc1ccc(cc1)C(F)(C)C

¹H NMR spectrum (CDCl₃) of 2-(4-cyanophenyl)-2-fluoropropane. The spectrum shows peaks at 7.80, 7.84, 7.82, 7.86 ppm (aromatic protons, integration 1.98, 1.99), 2.87, 2.80 ppm (methyl protons, integration 2.00), and 1.36, 1.31 ppm (methyl protons, integration 6.00).

126 MHz ^{13}C -NMR of 4-(2-fluoro-2-methylpropyl)benzonitrile (**29**) in CDCl_3

126 MHz ^{13}C -NMR of 4-(2-fluoro-2-methylpropyl)benzonitrile (**29**) in CDCl_3

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (**41**) in CDCl_3

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (**41**) in CDCl_3

500 MHz ^1H -NMR of 2-((4-fluoro-4-methylpentyl)oxy)-1,4-dimethylbenzene (**30**) in CDCl_3

126 MHz ^{13}C -NMR of 2-((4-fluoro-4-methylpentyl)oxy)-1,4-dimethylbenzene (**30**) in CDCl_3

376 MHz ^{19}F -NMR of 2-((4-fluoro-4-methylpentyl)oxy)-1,4-dimethylbenzene (**30**) in CDCl_3

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl (2*S*,4*aS*,6*aS*,6*bR*,12*aS*,12*bR*,14*bR*)-2,4*a*,6*a*,6*b*,9,9,12*a*-heptamethyl-10,13-dioxo-1,2,3,4,4*a*,5,6,6*a*,6*b*,7,8,8*a*,9,10,11,12,12*a*,12*b*,13,14*b*-icosahydricene-2-carboxylate (**S25**) in CDCl_3

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl (2*S*,4*aS*,6*aS*,6*bR*,12*aS*,12*bR*,14*bR*)-2,4*a*,6*a*,6*b*,9,9,12*a*-heptamethyl-10,13-dioxo-1,2,3,4,4*a*,5,6,6*a*,6*b*,7,8,8*a*,9,10,11,12,12*a*,12*b*,13,14*b*-icosahydricene-2-carboxylate (**S25**) in CDCl_3

500 MHz ^1H -NMR of (4a*R*,6a*R*,6b*S*,8a*S*,12a*R*,14a*R*,14b*S*)-11-fluoro-4,4,6a,6b,8a,11,14b-heptamethyl-1,2,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,14a,14b-octadecahydronicene-3,14-dione (**31**) in CDCl_3

126 MHz ^{13}C -NMR of (4*aR*,6*aR*,6*bS*,8*aS*,12*aR*,14*aR*,14*bS*)-11-fluoro-4,4,6*a*,6*b*,8*a*,11,14*b*-heptamethyl-1,2,4,4*a*,5,6,6*a*,6*b*,7,8,8*a*,9,10,11,12,12*a*,14*a*,14*b*-octadecahydricene-3,14-dione (**31**) in CDCl_3

282 MHz ^{19}F -NMR of (4a*R*,6a*R*,6b*S*,8a*S*,12a*R*,14a*R*,14b*S*)-11-fluoro-4,4,6a,6b,8a,11,14b-heptamethyl-1,2,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,14a,14b-octadecahydronicene-3,14-dione (**31**) in CDCl_3

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl 2-(4-(tert-butyl)phenoxy)acetate (**S26**) in CDCl_3

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl 2-(4-(tert-butyl)phenoxy)acetate (**S26**) in CDCl_3

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl 2-(4-(tert-butyl)phenoxy)acetate (**32**) in CDCl_3

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl 2-((4-bromophenyl)thio)acetate (**S27**) in CDCl_3

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl 2-((4-bromophenyl)thio)acetate (**S27**) in CDCl_3

500 MHz ^1H -NMR of (4-bromophenyl)(fluoromethyl)sulfane (**33**) in CDCl_3

126 MHz ^{13}C -NMR of (4-bromophenyl)(fluoromethyl)sulfane (**33**) in CDCl_3

282 MHz ^{19}F -NMR of (4-bromophenyl)(fluoromethyl)sulfane (**33**) in CDCl_3

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl (3*aS*,4*S*,6*R*,6*aR*)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxole-4-carboxylate (**S28**) in CDCl_3

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl (3*aS*,4*S*,6*R*,6*aR*)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxole-4-carboxylate (**S28**) in CDCl_3

500 MHz ^1H -NMR of (3*aR*,4*R*,6*R*,6*aS*)-4-(benzyloxy)-6-fluoro-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxole (**34**) in CDCl_3

126 MHz ^{13}C -NMR of (3a*R*,4*R*,6*R*,6a*S*)-4-(benzyloxy)-6-fluoro-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxole (**34**) in CDCl_3

470 MHz ^{19}F -NMR of (3a*R*,4*R*,6*R*,6a*S*)-4-(benzyloxy)-6-fluoro-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxole (**34**) in CDCl_3

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate (**S29**) in CDCl_3

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate (**S29**) in CDCl_3

500 MHz ^1H -NMR of (4-chlorophenyl)(4-((2-fluoropropan-2-yl)oxy)phenyl)methanone (**35**) in CDCl_3

126 MHz ^{13}C -NMR of (4-chlorophenyl)(4-((2-fluoropropan-2-yl)oxy)phenyl)methanone (**35**) in CDCl_3

470 MHz ^{19}F -NMR of (4-chlorophenyl)(4-((2-fluoropropan-2-yl)oxy)phenyl)methanone (**35**) in CDCl_3

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl 2-(4-(4-cyano-2-fluorophenoxy)phenoxy)propanoate (**S30**) in CDCl_3

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl 2-(4-(4-cyano-2-fluorophenoxy)phenoxy)propanoate (**S30**) in CDCl_3

282 MHz ^{19}F -NMR of 1,3-dioxoisindolin-2-yl 2-(4-(4-cyano-2-fluorophenoxy)phenoxy)propanoate (**S30**) in CDCl_3

500 MHz ^1H -NMR of 3-fluoro-4-(4-(1-fluoroethoxy)phenoxy)benzonitrile (**36**) in CD_2Cl_2

500 MHz ^1H -NMR 1,3-dioxoisindolin-2-yl 2-([1,1'-biphenyl]-4-yl)-2-fluoroacetate (**S31**) in CDCl_3

126 MHz ^{13}C -NMR 1,3-dioxoisindolin-2-yl 2-([1,1'-biphenyl]-4-yl)-2-fluoroacetate (**S31**) in CDCl_3

Chemical structure: O=C(O)c1cc2cc3ccccc3cc2cc1F

¹⁹F NMR spectrum (ppm):

- Peak at -179.26 ppm (integration 1.00)
- Peak at -179.09 ppm (integration 1.00)

[illegible]

126 MHz ^{13}C -NMR 4-(difluoromethyl)-1,1'-biphenyl (**37**) in CDCl_3

126 MHz ^{19}F -NMR 4-(difluoromethyl)-1,1'-biphenyl (**37**) in CDCl_3

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl 3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (**S32**) in CDCl_3

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl 3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (**S32**) in CDCl_3

282 MHz ^{19}F -NMR of 1,3-dioxoisindolin-2-yl 3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (**S32**) in CDCl_3

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl 9-fluoro-9H-fluorene-9-carboxylate (**S33**) in CDCl_3

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl 9-fluoro-9H-fluorene-9-carboxylate (**S33**) in CDCl_3

282 MHz ^{19}F -NMR 1,3-dioxoisindolin-2-yl 9-fluoro-9H-fluorene-9-carboxylate (**S33**) in CDCl_3

500 MHz ^1H -NMR of 9,9-difluoro-9H-fluorene (**39**) in CDCl_3

126 MHz ^{13}C -NMR of 9,9-difluoro-9*H*-fluorene (**39**) in CDCl_3

282 MHz ^{19}F -NMR of 9,9-difluoro-9*H*-fluorene (**39**) in CDCl_3

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl (2-phenylpropan-2-yl) oxalate (**S34**) in CDCl_3

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl (2-phenylpropan-2-yl) oxalate (**S34**) in CDCl_3

500 MHz ^1H -NMR of 1,3-dioxoisindolin-2-yl (2-methyl-4-phenylbutan-2-yl) oxalate (**S35**) in CDCl_3

126 MHz ^{13}C -NMR of 1,3-dioxoisindolin-2-yl (2-methyl-4-phenylbutan-2-yl) oxalate (**S35**) in CDCl_3

500 MHz ^1H -NMR of (3-fluoro-3-methylbutyl)benzene (**40**) in CDCl_3

75 MHz ^{19}F -NMR of (3-fluoro-3-methylbutyl)benzene (**40**) in CDCl_3

CC(F)(C)CC1=CC=CC=C1

126 MHz ^{13}C -NMR of 2-methoxy-6-(1-(2,4,6-trimethoxyphenyl)ethyl)naphthalene (**45**) in CDCl_3

500 MHz ^1H -NMR of 2-methoxy-6-(1-phenoxyethyl)naphthalene (**46**) in CDCl_3

126 MHz ^1H -NMR of 2-methoxy-6-(1-phenoxyethyl)naphthalene (**46**) in CDCl_3

500 MHz ^1H -NMR of 2-methoxy-6-(1-methoxyethyl)naphthalene (**47**) in CDCl_3

126 MHz ^{13}C -NMR of 2-methoxy-6-(1-methoxyethyl)naphthalene (**47**) in CDCl_3

500 MHz ^1H -NMR of 2-(1-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)ethyl)-6-methoxynaphthalene (**48**) in CDCl_3

126 MHz ^{13}C -NMR of 2-(1-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)ethyl)-6-methoxynaphthalene (**48**) in CDCl_3

282 MHz ^{19}F -NMR of 2-(1-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)ethyl)-6-methoxynaphthalene (**48**) in CDCl_3

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