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Decarboxylative intramolecular arene alkylation using *N*-(acyloxy)phthalimides, an organic photocatalyst, and visible light

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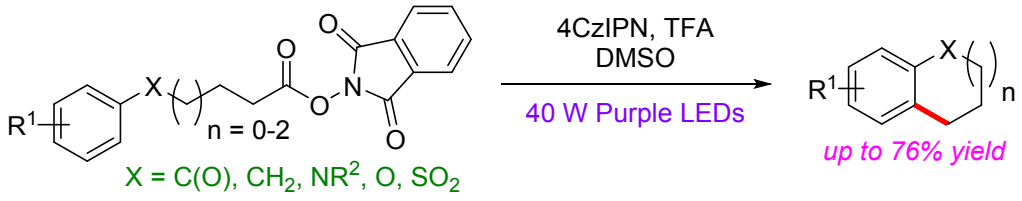
Supporting Information Placeholder

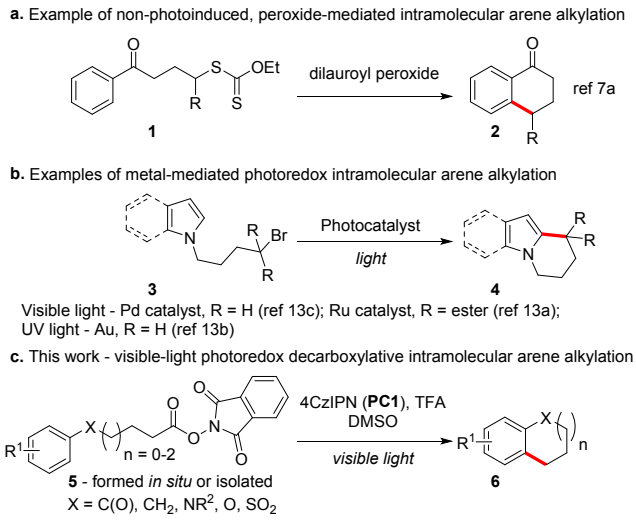


ABSTRACT: An intramolecular arene alkylation reaction has been developed using the organic photocatalyst 4CzIPN, visible light, and *N*-(acyloxy)phthalimides as radical precursors. Reaction conditions were optimized via high-throughput experimentation, and electron-rich and electron-deficient arenes and heteroarenes are viable reaction substrates. This reaction enables access to a diverse set of fused, partially saturated cores which are of high interest in synthetic and medicinal chemistry.

INTRODUCTION

The structural complexity of new molecular entities disclosed by pharmaceutical researchers continues to increase as is evident from the literature.[1] In order to enable chemists to continue to access novel scaffolds, the development of new methods for core synthesis, specifically cyclizations, are of paramount importance. Methods that enable the incorporation of sp^3-hybridized carbons are of specific interest to medicinal chemists as C(sp^3) incorporation can increase the three-dimensionality of pharmaceutical scaffolds, which is highly desirable.[2] In addition, alternate bond forming methods for the construction of partially saturated ring systems are of high interest to the chemistry community. Towards this end, we sought to develop a C(sp^3)-C(sp^2) cyclization reaction to give fused, partially saturated structures with good functional group tolerance. The intramolecular Friedel-Crafts reaction is a classical approach for carbon-carbon bond formation but typically requires harsh acidic conditions, is not highly functional group tolerant, and is limited to electron-rich arene substrates.[3] Radical chemistry,[4] on the other hand, is a well-appreciated complement to Friedel-Crafts chemistry,[5] with many radical-based reactions for intramolecular arene alkylation already established.[6-11] For example, alkyl halides[6] have been used in conjunction with tin reagents, peroxides, or transition metal catalysts for such cyclizations, as have alkyl xanthate esters (Scheme 1a)[7] under peroxide conditions. Photoredox chemistry[12] has seen some use for intramolecular arene alkylation with recent examples focused on pyrrole-containing scaffolds, alkyl halides, and transition metal photocatalysts (Scheme 1b).[13]

Scheme 1. Select methods for intramolecular arene alkylation



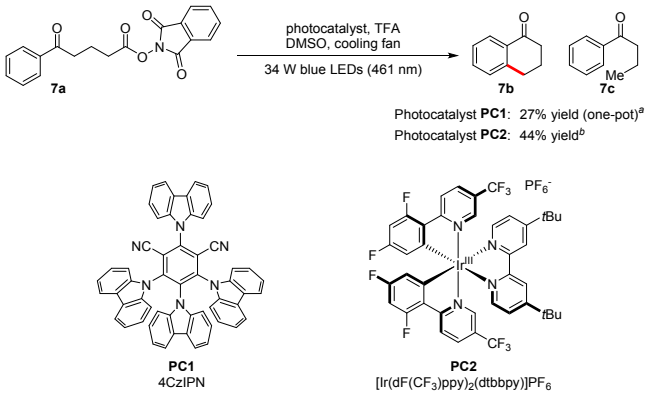
We recently disclosed an organocatalyzed, visible-light photoredox-mediated Minisci reaction using *in situ* prepared *N*-(acyloxyphthalimides) (NAPs) from carboxylic acids which has demonstrated a high degree of functional group tolerance.[14,15] We hypothesized that our Minisci method could be extended to

intramolecular arene alkylation if a radical formed from reductive fragmentation of generic NAP **5** could engage a tethered arene as shown in Scheme 1c. The alkyl radical should be particularly well-suited for reaction with electron-deficient arenes in close analogy to the Minisci reaction.[16] Given the requirement in Friedel-Crafts cyclizations for an electron-rich arene, our proposed reaction would be particularly attractive for use with electron-poor arenes for which Friedel-Crafts chemistry would be difficult. In contrast to typical Minisci processes, application to electron-rich arenes may be feasible, as well, due to the tethered nature of the reactive partners. While NAPs have recently seen widespread use,[17] to the best of our knowledge, our work disclosed herein is the first example employing NAPs for intramolecular arene alkylation under photoredox conditions.

RESULTS AND DISCUSSION

We began our studies targeting the synthesis of α-tetralone (**7b**, Scheme 2) as the ketone moiety provides an electron-deficient arene partner and can be used as a handle for post-cyclization modification. While there are examples of non-photoredox radical cyclizations for tetralone formation using xanthates[7a] or an alkyl halide,[6d] the peroxide conditions used can lead to product degradation if the reaction is not closely monitored. Application of our mild Minisci conditions would avoid such an undesired side reaction.

Scheme 2. Proof-of-concept experiments

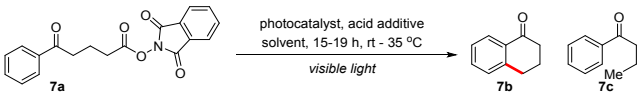


[a]Yield on 0.25 mmol scale with *in situ* formation of **7a** telescoped into photochemistry with **PC1** (1 mol %), TFA (1.5 equiv) in DMSO (0.13 M) irradiating for 8.5 h. [b]Yield on 0.25 mmol scale with **7a** (1.0 equiv), **PC2** (1 mol %), TFA (1.5 equiv) in DMSO (0.1 M) irradiating for 17 h without a cooling fan.

Initial proof-of-concept experiments applying our Minisci conditions using Kessil 34 W blue LEDs (461 nm) demonstrated that our envisioned cyclization was possible. α-Tetralone (**7b**) was obtained in modest but encouraging yields using either chromatographically pure NAP **7a** with 1 mol % of $[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$ (**PC2**, $E_{1/2}^{IV/III*}$ = –0.89 V vs SCE)[18] or *in situ* generated **7a**[19] with 1 mol % of the organic photocatalyst 1,2,3,5-tetrakis(carbazol-9-yl)-4,6-dicyanobenzene (4CzIPN, **PC1**, $E_{1/2}^{PC+/PC*}$ = –1.04 V vs SCE).[20] With proof-of-concept realized, we shifted to a high-throughput experimentation (HTE) platform[21] using a Lumidox LED photomat to investigate the influence of various parameters such as solvent, concentration, photocatalyst, LED wavelength, and acid additive on reaction outcome (select examples shown in Table 1, more examples in Tables S1 – S4), optimizing for formation of **7b**, ratio of cyclized to uncyclized **7b**:**7c**, and consumption of starting material **7a**.

Our HTE began with a broad screen of photocatalysts under blue light (470 nm) irradiation examining Ru and Ir complexes,[18] as well as organic photocatalysts.[22] As expected based on our proof-of-concept experiments, Ir complex **PC2** with TFA (1.5 equiv) provided desired **7b** with a favorable ratio of **7b**:**7c** and complete consumption of **7a** (entry 1). Running the reaction with 1 mol % of **PC1** gave similar results (entry 2) to **PC2**. While a variety of Ir complexes proved effective, other organic photocatalysts and Ru complexes gave unfavorable results with a significant amount of **7a** remaining unconsumed (see Table S1). Therefore, select Ir complexes as well as **PC1** were chosen for further optimization. Decreasing the loading of **PC1** to 0.5 mol % (entry 3) maintained reaction efficiency, although throughput with Ir complex **PC2** suffered with reduced loading.

Table 1. Select HTE entries optimizing the formation of α-tetralone (7b)[a]



entry	PC	acid (equiv)	light (nm)	AP of **7b**[a]	AP of **7a**[a]	**7b**:**7c**[a]
1	**PC2**[b]	TFA (1.5)	**470**	74	0.17	88:12
2	**PC1**[b]	TFA (1.5)	**470**	74	0.42	88:12
3	**PC1**	TFA (1.5)	**470**	73	0.25	87:13
4	**PC1**	TFA (1.5)	**527**	15	79	86:14
5	**PC1**	TFA (1.5)	white	64	14	88:12
6[c]	**PC1**	TFA (1.5)	**415**	73	0.24	87:13
7	**PC1**	BF_3•OEt_2 (1.5)	**470**	59	21	87:13
8[c]	**PC1**	BF_3•OEt_2 (1.5)	**415**	72	0.21	86:14
9	**PC1**	TFA (1.0)	**415**	67	5.10	85:15
10[d]	**PC1**	TFA (1.0)	**415**	61	26	93:7
11[d]	**PC1**	TFA (10)	**415**	81	4.5	94:6
12[d]	**PC3**	TFA (1.0)	**415**	80	0.70	91:9
13	**PC1**	-	**415**	23	62[e]	77:23
14	-	TFA (3.0)	**415**	<5	91	n/a
15	-	-	**415**	<5	95[e]	n/a

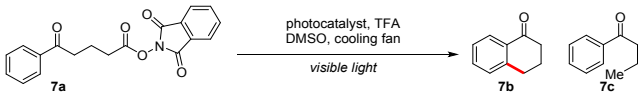
[a]Conversions and ratios obtained on reactions run on 0.010 mmol scale with NAP (**7a**, 1.0 equiv), acid additive, and PC (0.5 mol %) in DMSO (0.1 M) quantified by relative area percent (AP) of **7a**, **7b**, and **7c** from UHPLC analysis of the crude reaction mixture with UV detection at 254 nm. [b]1 mol % PC. [c]Reaction run at 0.08 M. [d]Reaction run at 0.02 M. [e]Combined AP of **7a** plus related material derived from unreacted **7a** under UHPLC analysis conditions. PC = photocatalyst.

Exploring the wavelength of light used, green (527 nm, entry 4) and white (entry 5) LEDs gave sluggish consumption of **7a**. Alternatively, purple (415 nm, entry 6) LEDs provided comparable performance to blue LEDs under several sets of conditions with select sets of conditions (one example shown in entries 7 and 8) providing enhanced rate of consumption of **7a** with the ratio of **7b**:**7c** unchanged. For this reason, purple LEDs were selected for subsequent optimization. As is evident from entries 7 and 8, acid additives besides TFA were viable in the

reaction[23] (see Table S2). Additionally, a screen of other polar solvents demonstrated that DMSO was indeed the most effective medium for this reaction (See Tables S3 and S4).

Investigating the effect of concentration (entries 9 – 12), it was found that improved ratios of **7b**:**7c** could be obtained by running the reaction at higher dilution (0.02 M). Incomplete conversion was noted with stoichiometric TFA and catalyst **PC1** (entry 10), but excess TFA (entry 11) was found to enhance the rate of conversion and maintain the favorable ratio of products with **PC1**. Additionally, select Ir catalysts, like $[Ir(dF(Me)ppy)_2(dtbbpy)]PF_6$ (**PC3**),[24] were found to give complete consumption of **7a** and comparable product ratios to **PC1** at high dilution (entry 12) with 1 equivalent of TFA.

Table 2. Optimization reactions on preparative scale for the formation of α-tetralone (7b)[a]

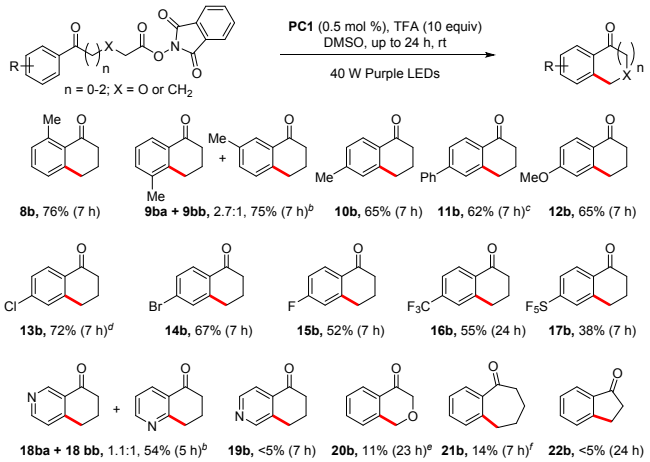


entry	PC	equiv TFA	light (nm)	time (h)	**7b**:**7c**[b]	yield (%) of **7b**
1[c]	**PC2**[d]	1.5	**461**	17	83:17	44
2[e]	**PC1**[d]	1.5	**461**	8.5	-	27
3	**PC1**	10	**427**	7	91:9	66
4	**PC1**	10	**461**	24	90:10	66
5	**PC3**	1.0	**427**	4.5[f]	83:17	55
6[g]	**PC1**	10	**427**	7	87:13	45
7[h]	**PC1**	10	**427**	7	85:15	58
8[i]	**PC1**	10	dark	7	n/a	ND[j]
9[k]	**PC1**	10	**427**	7	n/a	ND
10[l]	**PC1**	10	**427**	7	n/a	ND

[a]Yields on 0.5 mmol scale, standard conditions found in entry 3: **7a** (1.0 equiv), 4CzIPN (**PC1**, 0.5 mol %), TFA (10 equiv) in DMSO (0.02 M) with Kessil 40 W purple LED (427 nm) irradiation. Deviations from standard conditions for other entries noted in the table. Entries 1 and 2 repeated from Scheme 1. [b]Ratios determined by ^{1}H NMR of the crude reaction mixture, not determined for entry 2. [c]0.25 mmol scale at 0.1 M, no cooling fan used. [d]1 mol % PC. [e]**7a** formed *in situ* with excess DIC, 0.13 M in photochemistry. [f]**7a** fully consumed at 3 h but irradiated for 4.5 h. [g]**7a** formed *in situ* with stoichiometric reagents for esterification, 0.02 M in photochemistry. [h]**7a** formed *in situ* with excess reagents for esterification, 0.02 M in photochemistry. [i]0.25 mmol scale. [j]ND = not detected by LCMS. [k]**7a** replaced with corresponding carboxylic acid and *N*-hydroxyphthalimide. [l]**7a** replaced with corresponding carboxylic acid. PC = photocatalyst

Transitioning our work from HTE to preparative scale (Table 2), a favorable shift in the ratio of **7b**:**7c** and a 1.5-fold improvement in yield of **7b** was observed when comparing an initial proof-of-concept experiment (Table 2, entry 1) to post-HTE standard optimized conditions using photocatalyst **PC1** with Kessil 40 W purple LEDs (427 nm, entry 3, standard conditions).[25] The enhanced rate observed in the HTE for purple LEDs was also observed when comparing photocatalyst **PC1** with Kessil 34 W blue LEDs (entry 4) and entry 3. Although the yields are identical for purple and blue LED irradiation, only partial consumption of **7a** was observed at 7 h for blue LEDs with full conversion noted after 24 h. Quicker consumption of starting material was observed with **PC3** and 1 equivalent of TFA (entry 5), although the yield was lower. Nevertheless, this demonstrates that the reaction is feasible at low loadings of TFA with an alternative catalyst, which should enable acid-sensitive substrates to be viable participants in our reaction. Applying our optimized conditions to a one-pot process with *in situ* NAP formation, we tried both stoichiometric (entry 6) and slight excess (entry 7) loadings of the reagents used for the formation of **7a**. NAP formation was incomplete for entry 6 and trace carboxylic acid remained for entry 7, which may explain the slightly diminished yields for the one-pot processes. Nevertheless, entry 7 is a greater than 2-fold increase in yield over entry 2, a one-pot process performed prior to HTE optimization, and demonstrates that a one-pot process exhibits only modest decrease in throughput relative to its non-telescoped variant. Such a one-pot procedure may be desired if a required NAP is unstable or difficult to isolate.

Scheme 3. Aryl ketone cyclization scope[a]



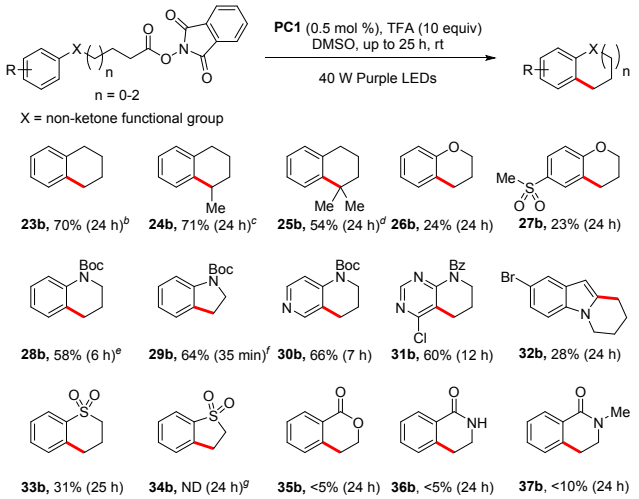
[a]Yields on 0.5 mmol scale following conditions from Table 2, entry 3. [b]Obtained as a mixture. [c]One-pot process with **11a** formed *in situ*. [d]Also run on 2.0 mmol scale in batch (65% yield, 7 h) and flow (57% yield, 2.5 mol % **PC1**; 70 min residence time). [e]0.25 mmol scale. [f]Also run with 34 W blue LEDs (461 nm): 15% (7 h).

Finally, control experiments in the HTE demonstrate that without TFA, reaction efficiency is significantly blunted, and without photocatalyst, essentially no reaction can occur (Table 1, entries 13 – 15). Additionally, controls run on preparative scale demonstrate that reaction run in the dark or with the unactivated carboxylic acid precursor to **7a** do not provide observable product (Table 2, entries 8 – 10).

Moving beyond the proof-of-concept substrate, we were pleased to find that electron-rich and electron-poor arenes were viable participants in our reaction. As shown in Scheme 3, substitution on the aryl ketone was tolerated. Products containing methyl groups were formed in good yield (**8b – 10b**). **9ba** and **9bb** were formed as a 2.7:1 ratio with the more congested product surprisingly favored for cyclization. Phenyl tetralone **11b** was made in a one-pot fashion in 62% yield from the corresponding carboxylic acid as NAP **11a** was difficult to isolate. Methoxy tetralone **12b** was formed in similar efficiency to α-tetralone (**7b**), as were halogenated tetralones **13b** and **14b**, demonstrating that cross-coupling handles for subsequent derivatization are tolerated and can be carried through our reaction without issue. Fluorine-containing tetralone **15b** was formed in slightly reduced efficiency. Electron-deficient trifluoromethyl substituted tetralone **16b** can be formed in 55% yield, requiring extended reaction time for completion, and

extremely electron-deficient pentafluorosulfaneyl tetralone **17b** can be formed in 38% yield.[26] Both **16b** and **17b** would likely be extremely difficult to synthesize with typical Friedel-Crafts chemistry and highlight an advantage of our method. Isomeric pyridine-containing products **18ba** and **18bb** were formed in 54% yield in only 5 h, but the related pyridine **19b** was not formed in significant quantity. **20b** was formed in low yield. Examining different ring sizes, 7-membered ketone **21b** was formed in 14% yield using standard conditions and was also formed in comparable yield within 7 h when irradiated with 34 W blue LEDs. Indanone (**22b**) was not formed in significant quantity.

Scheme 4. Non-ketone arene cyclization scope[a]



[a]Yields on 0.5 mmol scale following conditions from Table 2, entry 3. [b]NMR yield. [c]0.45 mmol scale. [d]0.44 mmol scale. [e]0.29 mmol scale, 12.5:1 ratio of **28b**:**28c**. [f]12.5:2.5:1 ratio of **29b**:**29c**:NBoc indole (**29d**), see Experimental Section. [g]ND = not detected by LCMS.

Non-ketone substrates worked as well, with electron-rich arenes proving viable reaction participants (Scheme 4). Tetralin (**23b**) was formed in good yield after 24 h, as were related methylated products resulting from α-methyl NAPs (**24b** and **25b**), demonstrating that secondary and tertiary radicals can be productively generated in this reaction. A phenolic ether was tolerated in the tether (**26b** and **27b**), although extended reaction time was required and modest yields were obtained. NBoc protected substrates **28b** and **29b** were formed in good yields with indoline formation being the fastest of all the substrates tested in this work, likely due to the favorable kinetics for 5-membered ring formation.[27] Heterocyclic products **30b** and **31b** were both formed in good yield. Notably, Boc removal was not observed for aryl carbamates **28b** – **30b**, highlighting the relative mildness of the reaction conditions even with 10 equivalents of TFA present. Tricyclic bromo-indole **32b** was formed in modest yield, as was 6-membered sulfone **33b.** Finally, 5-membered sulfone **34b**, lactone **35b**, and lactams **36b** and **37b** were not formed in significant quantity.

Exploring reaction performance on larger scales in batch and flow, we selected **13b** as an ideal test case due to the presence of a cross-coupling handle for potential use in post-cyclization chemistry. **13b** was formed in batch on 2.0 mmol scale in a flask setup identical to our 0.5 mmol standard conditions, giving comparable yield on both scales (0.5 mmol, 72% yield; 2.0 mmol, 65% yield) and no change in reaction time. **13b** was also formed on 2.0 mmol scale in slightly lower yield (57%) using a Vapourtec photochemical flow reactor with 60 W purple LEDs (420 nm), higher loading of **PC1** (2.5 mol %), and 70 min of photoreactor residence time in a 10 mL fluorinated ethylene polymer (FEP) tubing residence coil at 34 °C.

In a set of optimization experiments, it was determined that reaction performance (based on conversion profiles of the crude reaction mixtures) was more effective with 420 nm light than 440 nm light, and increased conversion was observed at 50 °C vs 34 °C (Figure 2). Experiments run with 10 min residence time experienced saturation in light with 0.5 mol % of **PC1**, and an increased photocatalyst loading (2.5 mol %) was used afterwards. Nearly 90% conversion was observed with 50 min residence time and 2.5 mol % **PC1**. Accordingly, to ensure sufficient conversion, we performed further batches at 70 min residence time, including the batch performed at 2.0 mmol scale. Overall, the desired transformation worked well in the continuous domain achieving identical performance at 0.1 and 2.0 mmol scale (20x scale-up), with future opportunity for further optimization (e.g. concentration, temperature).

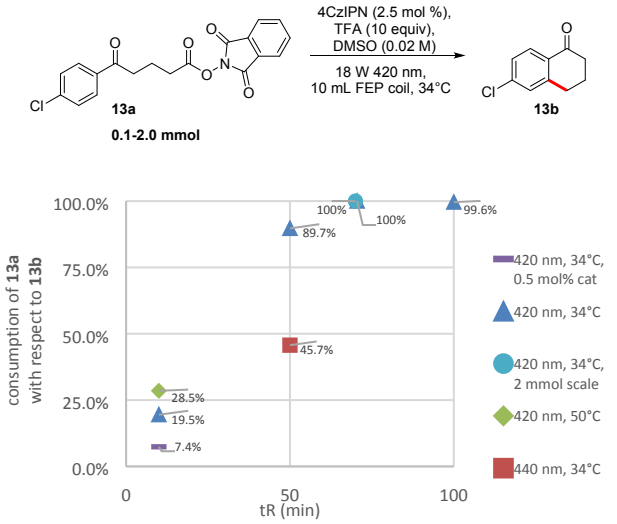


Figure 1. Study of conversion with respect to residence time under varying conditions. Conversion profile determined by UHPLC analysis of the crude reaction mixture with UV detection at 220 nm. Any deviations from standard conditions noted in chart legend.

To gain insight into the mechanism of the transformation, a series of luminescence quenching and cyclic voltammetry (CV) measurements were performed. First, a Stern-Volmer analysis in DMSO revealed that substrate **7a** does not quench the luminescence of **PC1** in the presence or absence of TFA. This suggests that the excited state of the photocatalyst is not sufficiently reducing to enable direct substrate activation by either electron transfer or proton-coupled electron transfer (PCET). CV measurements revealed that the reduction potential of **7a** is –1.06 V vs. SCE, yet this potential is positively shifted by ~40 mV upon addition of 10 equivalents of TFA, consistent with a possible PCET-based mechanism for reduction.[28] However, we observed the reduction potential of **PC1** to be –1.19 V vs. SCE, making reduction of **7a** by the **PC1** radical anion favorable. To confirm the feasibility of this elementary step, we carried out voltammetry on solutions containing **PC1**, **7a**, and TFA. While voltammograms of **PC1** alone were reversible, a strong catalytic current was observed when all

three species were present, as characterized by an earlier onset potential, increased current response, and lack of reversibility for the **PC1**/**PC1**$^{\bullet-}$ couple (Figure 2). Taken together these results suggest that reduction of **7a** likely occurs via a PCET mechanism mediated by TFA and the radical anion of **PC1**.

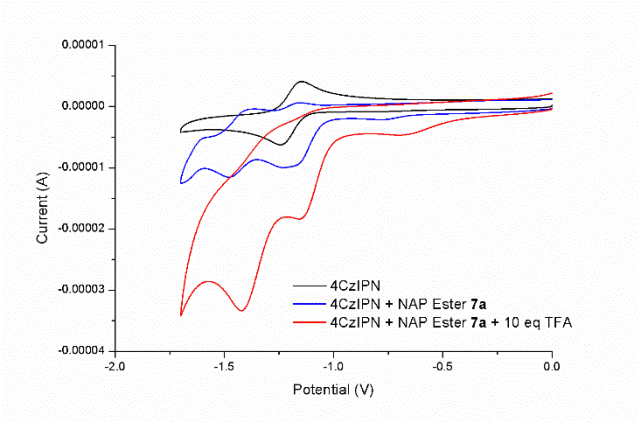


Figure 2. Overlay of the cyclic voltammogram of 4CzIPN upon addition of **7a** and TFA. Conditions: 1 mM **PC1**, 1 mM **7a**, and 10 mM TFA with 0.1 M tetrabutylammonium hexafluorophosphate. A glassy carbon working electrode, SCE reference electrode, and platinum mesh counter electrode were used. The experiment was conducted in DMSO at 23 °C with a scan rate of 0.1 V/s. Each voltammogram was obtained independently.

From these data, we considered two potential mechanisms. First, the reaction could be initiated by off-cycle reductive quenching of **PC1** to generate its radical anion, which in turn reduces the substrate followed to initiate fragmentation and cyclization. The resulting cyclohexadienyl radical **41** could propagate a radical chain pathway by reducing another molecule of **7a** either through PT/ET or HAT. With respect to the former, a Bordwell-type thermochemical cycle suggests the pK_a of the cyclohexadienyl radical is –2.6 in DMSO.[29] This low value indicates that the radical might be deprotonated even under the acidic reaction conditions to furnish a radical anion that could propagate the chain.[30] Similarly, the cyclohexadienyl radical was calculated to have a C-H bond strength of only 13.6 kcal/mol (CBS-QB3), suggesting that HAT-based propagation is also thermochemically favorable. The second mechanistic possibility would involve an on-cycle reduction of the photocatalyst by the cyclohexadienyl radical to both turn over the **PC1** cycle as well as form product **7b** following deprotonation (Figure 3). The reduction potential of the cyclohexadienyl radical of benzene has been previously reported[31] to be –0.344 V vs SCE and well within the range of 4CzIPN's excited state potential (+1.43 V vs. SCE).[32] To help distinguish between these two possibilities, we measured the quantum yield of the reaction of **7a** to be 0.022. The low quantum efficiency suggests that the reaction likely occurs via a closed catalytic cycle, though we cannot rule out the possibility of a poorly initiated chain reaction. Taken together, these results are consistent with the proposed catalytic cycle in Figure 3.

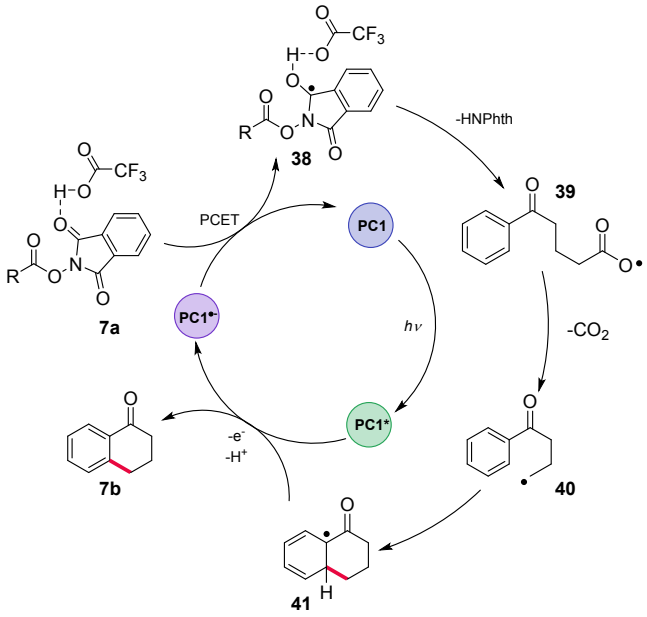


Figure 3. Proposed catalytic cycle for the synthesis of α-tetralone (**7b**)

CONCLUSION

In conclusion, we have developed a decarboxylative intramolecular arene alkylation utilizing NAPs as radical precursors with an organic photocatalyst and visible light. The reaction can be scaled in batch and flow and demonstrates good functional group tolerance with both electron-rich and electron-deficient arenes and heteroarenes being viable substrates. Our reaction is milder than typical Friedel-Crafts protocols and avoids the use of toxic heavy metals or peroxide reagents for radical generation. To the best of our knowledge, this is the first example of NAPs being used in a photoinduced, intramolecular arene C-H alkylation reaction. Overall, this cyclization method should enable access to a diverse set of fused cores and scaffolds for chemical research.

EXPERIMENTAL SECTION

General Information. Unless otherwise stated, reactions were run in standard glassware with rubber septa or in glass vials purchased from Chemglass with caps containing a teflon-lined septum. Reactions were monitored by liquid chromatography/mass spectrometry (LCMS) on a Waters Acquity UPLC BEH C18 column (2.1 × 50 mm, 1.7 µm); solvent A: water with 0.05% TFA, solvent B: acetonitrile with 0.05% TFA; gradient from 2% B to 98% B over 1.0 min then 98% B for 0.5 min, flow rate 0.8 mL/min, detection by UV at 220 nm and/or 254 nm and low resolution mass spectrometry detection with either Waters SQ Detector 2 with electrospray ionization (ESI) or Waters 3100 Detector with ESI (noted as "LCMS" below) or by LC alone on a Shimadzu UPLC Phenomenex Kinetix C18 column (2.1 × 50 mm, 2.6 µm); solvent A: 90% water/10% acetonitrile with 0.1% TFA, solvent B: 10% water/90% acetonitrile with 0.1% TFA; gradient from 0% B to 100% B over 1.5 min then 100% B for 0.5 min, flow rate 1 mL/min, detection by UV at 220 nm and/or 254 nm (noted as "LC" below). Flash column chromatography was performed on a Teledyne Isco instrument using redisep Rf silica columns and 40-63 µm silica gel from Fluka Analytical. Hexanes, EtOAc, DCM and MeOH used for purification were purchased

as UPLC grade. Analytical HPLC retention times, where noted, were obtained using a Shimadzu Scientific Instruments SIL-10AF HPLC with two columns: column 1: ACE Ucore Super C18 (3.0 × 125 mm, 2.5 μm) and column 2: ACE UCore SuperHexPh (3.0 × 125 mm, 2.5 μm); solvent A: 95% water/5% acetonitrile with 0.05% TFA, solvent B: 5% water/95% acetonitrile with 0.05% TFA; gradient from 10% B to 100% B over 12 minutes, held at 100% B from 12 to 15 minutes; flow rate 1 mL/min; detection at 220 nm and 254 nm. All solvents, reagents, and organic building blocks were purchased from commercial suppliers and used without further purification.

^{1}H and ^{13}C NMR spectra were obtained on Bruker Avance III HD and Avance NEO instruments at fields of 400 MHz and 500 MHz, equipped with either a 5mm BBFO Probe or a Prodigy BBO Probe. All NMR spectra were obtained at room temperature unless otherwise stated. NMR spectra were internally referenced to the solvent peak.[33] Chemical shifts are reported in parts per million (ppm). Data is reported in the following format: chemical shift (δ ppm), descriptor if applicable (br = broad, app = apparent), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, m = multiplet, spt = septet), coupling constant (Hz), integration. High resolution mass spectra (HRMS) were obtained on a ThermoFinnigan LTQ Orbitrap XL (ESI), ThermoFinnigan Orbitrap Exactive (ESI), or a Thermo Q Exactive Plus (ESI).

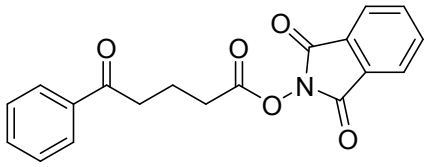
General Information for HTE. Microscale high-throughput experiments were carried out in a nitrogen-filled glovebox. A 96-well photoredox block (Analytical Sales and Services, Cat. No. 96973) was loaded with empty 1 mL borosilicate glass vials. Photoredox catalysts with limited solubility in DMSO were added as solutions or suspensions in an appropriate solvent (DCM or DCE) and then concentrated to dryness using a Genevac vacuum centrifuge. A micro stir bar was charged to each vial, then the remaining photoredox catalysts were added as DMSO solutions, followed by a solution of the NAP ester (10 μmol per vial) and then a solution of the appropriate additive. The photoredox block was sealed under N_2 with a sheet of PFA film, two rubber mats and a metal lid. The block was set on a Lumidox 96-well LED array (Analytical Sales and Services, LUM96B, LUM96BGW or LUM96-415) that was situated on a Freeslate CM3 automation system and controlled by a Lumidox controller (Analytical Sales and Services, LUMCON or LUMCON-UV). For more information about the LED array, please see the Analytical Sales and Services website. After irradiating at ambient temperature with tumble stirring for 15-19 h, the block was removed from the glovebox and unsealed. The reaction mixtures were diluted with MeOH, then filtered and analyzed by UPLCMS on a Waters Acquity BEH C8 column (2.1 × 50 mm, 1.7 μm); solvent A: 5:95 acetonitrile:water with 0.05% TFA, solvent B: 95:5 acetonitrile:water with 0.05% TFA; gradient from 0% B to 100% B over 2.0 min then 100% B for 0.5 min, flow rate 1.0 mL/min, detection by UV at 254 nm and low resolution mass spectrometry detection (positive ion mode) with a Shimadzu LCMS-2020 mass spectrometer.

General procedure for NAP formation. To a suspension of the appropriate carboxylic acid (3 mmol, 1 equiv), *N*-hydroxyphthalimide (808 mg, 4.95 mmol, 1.65 equiv), and DMAP (18 mg, 0.15 mmol, 0.05 equiv) in THF or DCM (15 mL, 0.2 M) was added DIC (0.70 mL, 4.5 mmol, 1.5 equiv). The reaction was stirred at room temperature for up to 3 days or until judged complete by LCMS analysis. The crude reaction mixture was then diluted with DCM and filtered through a pad of celite. The crude filtrate was concentrated and purified by silica gel column chromatography on a Teledyne Isco instrument to give the NAP after concentration of the desired fractions.

General procedure for intramolecular arene alkylation. To a solution of the NAP substrate (0.5 mmol, 1 equiv) and 4CzIPN (**PC1**, 2 mg, 2.5 μmol, 0.5 mol %) in DMSO (25 mL) in a 40 mL borosilicate glass vial with a pressure-relief septum and a stir bar was added TFA (0.38 mL, 5.0 mmol, 10 equiv). The resulting solution was degassed for 2-3 minutes with nitrogen gas, sealed, and placed above a stir plate in between two 40 W Kessil lamps model PR160 427 (purple light, λ_{max} = 427 nm) set to 100% and about 12 cm apart. An overhead cooling fan was used to keep the reaction at or near room temperature. For more information about the Kessil LED lamps, please see the Kessil website. The reaction was monitored by LCMS and degassed for ~60 seconds after reaction sampling before resuming irradiation in order to prevent sampling from introducing oxygen to the reaction vessel. Upon completion, the reaction was opened to air and worked up by pouring into a separatory funnel and diluting with 125 mL of DCM, 50 mL of 1.5 M aqueous K_2HPO_4 solution, and 100 mL of water. The biphasic mixture was shaken vigorously with venting. The organic layer was separated, washed with water (2x50 mL), dried over Na_2SO_4, filtered, and concentrated to afford crude material. Unless otherwise stated, the crude material was purified by silica gel column chromatography on a Teledyne Isco instrument to give final product after concentration of the desired fractions.

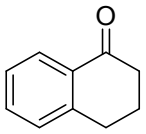
General procedure for one-pot NAP formation and intramolecular arene alkylation. To a solution of the appropriate carboxylic acid (0.5 mmol, 1 equiv), *N*-hydroxyphthalimide (106 mg, 0.65 mmol, 1.3 equiv), and DMAP (3 mg, 0.025 mmol, 0.05 equiv) in DMSO (2.5 mL, 0.2 M) in a 40 mL borosilicate glass vial with a pressure relief septum and a stir bar was added DIC (0.12 mL, 0.75 mmol, 1.5 equiv). The reaction was stirred at room temperature for up to 25 hours or until judged complete by LCMS analysis. Upon completion of NAP formation, DMSO (22.5 mL) was added to dilute the reaction to 0.02 M followed by TFA (0.38 mL, 5.0 mmol, 10 equiv) and 4CzIPN (**PC1**, 2 mg, 2.5 μmol, 0.5 mol %). The resulting solution was degassed for 2-3 minutes with nitrogen gas, sealed, and placed above a stir plate in between two 40 W Kessil lamps model PR160 427 (purple light, λ_{max} = 427 nm) set to 100% and about 12 cm apart. An overhead cooling fan was used to keep the reaction at or near room temperature. The reaction was monitored by LCMS and degassed for ~60 seconds after reaction sampling before resuming irradiation in order to prevent sampling from introducing oxygen to the reaction vessel. Upon completion, the reaction was opened to air and worked up by pouring into a separatory funnel and diluting with 125 mL of DCM, 50 mL of 1.5 M aqueous K_2HPO_4 solution, and 100 mL of water. The biphasic mixture was shaken vigorously with venting. The organic layer was separated, washed with water (2x50 mL), dried over Na_2SO_4, filtered, and concentrated to afford crude material. Unless otherwise stated, the crude material was purified by silica gel column chromatography on a Teledyne Isco instrument to give final product after concentration of the desired fractions.

Entries 1, 3 – 5, and 8 – 10 in Table 1 were run following the general procedure for intramolecular arene alkylation using NAP substrate **7a** (169 mg, 0.5 mmol, 1 equiv) with the noted modifications to scale (0.25 mmol for entries 1 and 8), concentration, photocatalyst, equivalents of TFA, light source, and/or reaction time. Entry 8 was wrapped in foil and stirred in the dark without LED irradiation. Entries 9 and 10 were not run with NAP substrate **7a** and instead used 5-oxo-5-phenylpentanoic acid (96 mg, 0.5 mmol, 1 equiv) alone (entry 10) or 5-oxo-5-phenylpentanoic acid (96 mg, 0.5 mmol, 1 equiv) and *N*-hydroxyphthalimide (82 mg, 0.5 mmol, 1 equiv) together (entry 9). Entry 6 followed the general procedure for one-pot NAP formation and intramolecular arene alkylation using *N*-hydroxyphthalimide (82 mg, 0.5 mmol, 1 equiv) and DIC (0.078 mL, 0.5 mmol, 1 equiv) and stirring for 18 h for NAP formation. Entry 7 followed the general procedure for one-pot NAP formation and intramolecular arene alkylation using *N*-hydroxyphthalimide (90 mg, 0.55 mmol, 1.1 equiv) and stirring for 18 h for NAP formation. Entry 2 was run as follows: To a solution of 5-oxo-5-phenylpentanoic acid (100 mg, 0.52 mmol, 1 equiv), *N*-hydroxyphthalimide (85 mg, 0.52 mmol, 1 equiv), and DMAP (3.2 mg, 0.026 mmol, 0.05 equiv) in DMSO (4 mL, 0.13 M) was added DIC (0.081 mL, 0.52 mmol, 1 equiv). After stirring 17 h, another aliquot of DIC (0.081 mL, 0.52 mmol, 1 equiv) was added and the reaction was again stirred 24 h. Then, TFA (0.060 mL, 0.78 mL, 1.5 equiv) was added followed by 4CzIPN (**PC1**, 4.1 mg, 5.2 µmol, 1 mol %). The resulting solution was degassed for 1 minute with nitrogen gas, sealed, and placed above a stir plate in between two Kessil 34 W KSH150B grow light LEDs (blue light, λ_{max} = 461 nm) about 12 cm apart. An overhead cooling fan was used to keep the reaction at or near room temperature. For more information about the Kessil LED lamps, please see the Kessil website. The reaction was stirred with irradiation for 8.5 h. Upon completion, the reaction was diluted with water and extracted with a mixture of hexanes and diethyl ether. The organic layer was concentrated. Silica gel column chromatography on a Teledyne Isco instrument and concentration of the desired fractions afforded the desired product α-tetralone (**7b**, 20.7 mg, 27% yield).



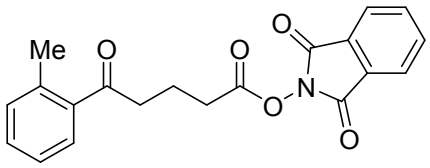
7a

1,3-dioxoisoindolin-2-yl 5-oxo-5-phenylpentanoate (7a). NAP prepared by the general procedure for NAP formation using 5-oxo-5-phenylpentanoic acid (1.5 g, 7.8 mmol, 1 equiv), *N*-hydroxyphthalimide (2.1 g, 12.9 mmol, 1.65 equiv), DMAP (49 mg, 0.40 mmol, 0.05 equiv), DIC (1.82 mL, 11.7 mmol, 1.5 equiv), and THF (39 mL) stirring for 44.5 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 5-oxo-5-phenylpentanoate (**7a**, 2.3 g, 87% yield) as an off-white solid. LCMS t_r = 0.94 min; ^{1}H NMR (499 MHz, CHLOROFORM-d) δ 8.03 - 7.98 (m, 2H), 7.92 - 7.87 (m, 2H), 7.82 - 7.78 (m, 2H), 7.60 - 7.55 (m, 1H), 7.51 - 7.46 (m, 2H), 3.20 (t, *J*=7.0 Hz, 2H), 2.84 (t, *J*=7.0 Hz, 2H), 2.25 (quin, *J*=7.1 Hz, 2H); ^{13}C{^{1}H} NMR (126 MHz, CHLOROFORM-d) δ 199.0, 169.5, 162.1, 136.9, 134.9, 133.3, 129.1, 128.8, 128.2, 124.2, 36.9, 30.4, 19.3; HRMS (ESI) *m/z* calcd for $C_{19}H_{16}NO_5$ [M+H$^+$] 338.1023, found 338.1026.



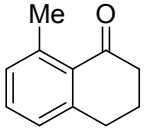
7b

α-tetralone (7b). Cyclization product prepared by the general procedure for intramolecular arene alkylation using **7a** (169 mg, 0.5 mmol, 1 equiv), 4CzIPN (**PC1**, 2 mg, 2.5 µmol, 0.5 mol %), and TFA (0.38 mL, 5.0 mmol, 10 equiv) in DMSO (25 mL) irradiating with purple light for 7 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave α-tetralone (**7b**, 48 mg, 66% yield) as a light yellow oil. LCMS t_r = 0.81 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 8.03 (d, *J*=7.8 Hz, 1H), 7.47 (td, *J*=7.4, 1.2 Hz, 1H), 7.30 (t, *J*=7.6 Hz, 1H), 7.25 (d, *J*=7.9 Hz, 1H), 2.97 (t, *J*=6.1 Hz, 2H), 2.69 - 2.62 (m, 2H), 2.19 - 2.09 (m, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 198.5, 144.6, 133.5, 132.8, 128.9, 127.3, 126.7, 39.3, 29.8, 23.4; HRMS (ESI) *m/z* calcd for $C_{10}H_{11}O$ [M+H$^+$] 147.0804, found 147.0806.



8a

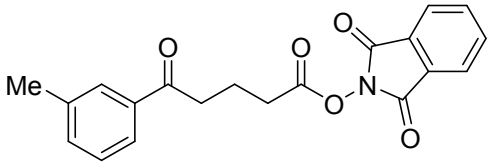
1,3-dioxoisoindolin-2-yl 5-oxo-5-(*o*-tolyl)pentanoate (8a). NAP prepared by the general procedure for NAP formation using 5-oxo-5-(*o*-tolyl)pentanoic acid (412 mg, 2.0 mmol, 1 equiv), *N*-hydroxyphthalimide (538 mg, 3.30 mmol, 1.65 equiv), DMAP (12 mg, 0.10 mmol, 0.05 equiv), DIC (0.47 mL, 3.0 mmol, 1.5 equiv), and THF (10 mL) stirring for 71 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 5-oxo-5-(*o*-tolyl)pentanoate (**8a**, 475 mg, 68% yield) as a white solid. LCMS t_r = 0.99 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.92 - 7.86 (m, 2H), 7.82 - 7.76 (m, 2H), 7.71 (dd, *J*=7.8, 0.6 Hz, 1H), 7.38 (td, *J*=7.4, 1.2 Hz, 1H), 7.31 - 7.22 (m, 2H), 3.12 (t, *J*=7.1 Hz, 2H), 2.82 (t, *J*=7.0 Hz, 2H), 2.52 (s, 3H), 2.22 (quin, *J*=7.1 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 202.9, 169.5, 162.1, 138.4, 137.7, 134.9, 132.2, 131.6, 129.1, 128.8, 126.0, 124.2, 39.7, 30.4, 21.5, 19.4; HRMS (ESI) *m/z* calcd for $C_{20}H_{17}NO_5Na$ [M+Na$^+$] 374.0999, found 374.1004.



8b

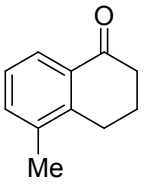
8-methyl-3,4-dihydronaphthalen-1(2*H*)-one (8b). Cyclization product prepared by the general procedure for intramolecular arene alkylation using **8a** (176 mg, 0.5 mmol, 1 equiv), 4CzIPN (**PC1**, 2 mg, 2.5 µmol, 0.5 mol %), and TFA (0.38 mL, 5.0 mmol, 10 equiv) in DMSO (25 mL) irradiating with purple light for 7 h. Purification by flash column

chromatography using silica gel on a Teledyne Isco instrument gave 8-methyl-3,4-dihydronaphthalen-1(2*H*)-one (**8b**, 61 mg, 76% yield) as a clear oil. LCMS t_r = 0.89 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.30 (t, *J*=7.5 Hz, 1H), 7.14 - 7.05 (m, 2H), 2.96 (t, *J*=6.1 Hz, 2H), 2.67 - 2.62 (m, 5H), 2.13 - 2.04 (m, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 200.3, 145.8, 141.6, 132.3, 131.4, 130.6, 126.9, 41.1, 31.2, 23.4, 23.2; HRMS (ESI) *m/z* calcd for $C_{11}H_{13}O$ [M+H$^+$] 161.0961, found 161.0964.

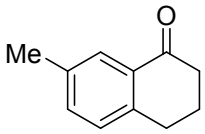


9a

1,3-dioxoisoindolin-2-yl 5-oxo-5-(*m*-tolyl)pentanoate (9a). NAP prepared by the general procedure for NAP formation using 5-oxo-5-(*m*-tolyl)pentanoic acid (619 mg, 3.0 mmol, 1 equiv), *N*-hydroxyphthalimide (808 mg, 4.95 mmol, 1.65 equiv), DMAP (18 mg, 0.15 mmol, 0.05 equiv), DIC (0.70 mL, 4.5 mmol, 1.5 equiv), and THF (15 mL) stirring for 16 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 5-oxo-5-(*m*-tolyl)pentanoate (**9a**, 836 mg, 79% yield) as a white solid. LCMS t_r = 0.97 min; ^{1}H NMR (499 MHz, CHLOROFORM-d) δ 7.92 - 7.87 (m, 2H), 7.83 - 7.77 (m, 4H), 7.41 - 7.34 (m, 2H), 3.18 (t, *J*=7.1 Hz, 2H), 2.83 (t, *J*=7.0 Hz, 2H), 2.42 (s, 3H), 2.24 (quin, *J*=7.1 Hz, 2H); ^{13}C{^{1}H} NMR (126 MHz, CHLOROFORM-d) δ 199.2, 169.5, 162.1, 138.6, 136.9, 134.9, 134.1, 129.1, 128.8, 128.7, 125.5, 124.1, 37.0, 30.4, 21.5, 19.3; HRMS (ESI) *m/z* calcd for $C_{20}H_{18}NO_5$ [M+H$^+$] 352.1179, found 352.1184.

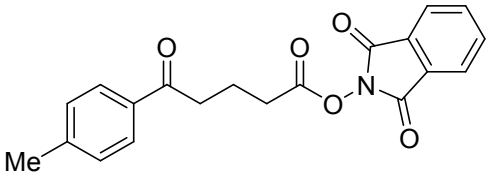


9ba



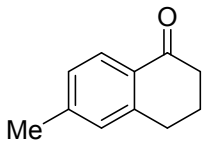
9bb

5-methyl-3,4-dihydronaphthalen-1(2*H*)-one (9ba) and 7-methyl-3,4-dihydronaphthalen-1(2*H*)-one (9bb). Cyclization products prepared by the general procedure for intramolecular arene alkylation using **9a** (176 mg, 0.5 mmol, 1 equiv), 4CzIPN (**PC1**, 2 mg, 2.5 µmol, 0.5 mol %), and TFA (0.38 mL, 5.0 mmol, 10 equiv) in DMSO (25 mL) irradiating with purple light for 7 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 5-methyl-3,4-dihydronaphthalen-1(2H)-one (**9ba**) and 7-methyl-3,4-dihydronaphthalen-1(2*H*)-one (**9bb**) as a mixture in a 2.7:1 ratio of **9ba**:**9bb** (60 mg, 75% yield) as a yellow oil. LCMS t_r = 0.86 min (major isomer **9ba**) and 0.88 (minor isomer **9bb**); Major isomer **9ba**: ^{1}H NMR (499 MHz, CHLOROFORM-d) δ 7.92 (d, *J*=7.9 Hz, 1H), 7.35 (d, *J*=7.4 Hz, 1H), 7.21 (t, *J*=7.6 Hz, 1H), 2.86 (t, *J*=6.1 Hz, 2H), 2.67 - 2.61 (m, 2H), 2.31 (s, 3H), 2.19 - 2.12 (m, 2H); Minor isomer **9bb**: ^{1}H NMR (499 MHz, CHLOROFORM-d) δ 7.84 (s, 1H), 7.28 (app d, *J*=7.7 Hz, 1H), 7.14 (d, *J*=7.7 Hz, 1H), 2.92 (t, *J*=6.0 Hz, 2H), 2.67 - 2.61 (m, 2H), 2.36 (s, 3H), 2.16 - 2.08 (m, 2H); Carbon NMR peaks were not assigned to individual isomers: ^{13}C{^{1}H} NMR (126 MHz, CHLOROFORM-d) δ 198.9, 198.8, 142.9, 141.8, 136.5, 136.4, 134.9, 134.5, 133.0, 132.5, 128.8, 127.4, 126.2, 125.2, 39.4, 38.8, 29.5, 26.6, 23.6, 22.7, 21.1, 19.7; HRMS (ESI) *m/z* calcd for $C_{11}H_{13}O$ [M+H$^+$] 161.0961, found 161.0964.



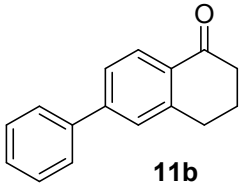
10a

1,3-dioxoisoindolin-2-yl 5-oxo-5-(*p*-tolyl)pentanoate (10a). NAP prepared by the general procedure for NAP formation using 5-oxo-5-(*p*-tolyl)pentanoic acid (619 mg, 3.0 mmol, 1 equiv), *N*-hydroxyphthalimide (808 mg, 4.95 mmol, 1.65 equiv), DMAP (18 mg, 0.15 mmol, 0.05 equiv), DIC (0.70 mL, 4.5 mmol, 1.5 equiv), and THF (15 mL) stirring for 19.5 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 5-oxo-5-(*p*-tolyl)pentanoate (**10a**, 810 mg, 77% yield) as an off-white solid. LCMS t_r = 0.98 min; ^{1}H NMR (499 MHz, CHLOROFORM-d) δ 7.93 - 7.87 (m, 4H), 7.82 - 7.77 (m, 2H), 7.29 - 7.25 (m, 2H), 3.17 (t, *J*=7.1 Hz, 2H), 2.82 (t, *J*=7.0 Hz, 2H), 2.41 (s, 3H), 2.24 (quin, *J*=7.1 Hz, 2H); ^{13}C{^{1}H} NMR (126 MHz, CHLOROFORM-d) δ 198.6, 169.5, 162.1, 144.1, 134.9, 134.4, 129.5, 129.1, 128.4, 124.1, 36.8, 30.4, 21.8, 19.4; HRMS (ESI) *m/z* calcd for $C_{20}H_{18}NO_5$ [M+H$^+$] 352.1179, found 352.1184.



10b

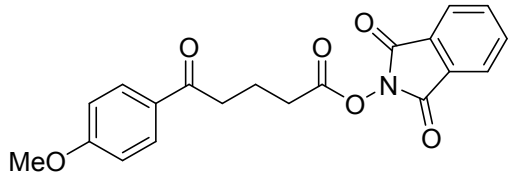
6-methyl-3,4-dihydronaphthalen-1(2*H*)-one (10b). Cyclization product prepared by the general procedure for intramolecular arene alkylation using **10a** (176 mg, 0.5 mmol, 1 equiv), 4CzIPN (**PC1**, 2 mg, 2.5 µmol, 0.5 mol %), and TFA (0.38 mL, 5.0 mmol, 10 equiv) in DMSO (25 mL) irradiating with purple light for 7 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 6-methyl-3,4-dihydronaphthalen-1(2*H*)-one (**10b**, 52 mg, 65% yield) as a light yellow oil. LCMS t_r = 0.87 min; ^{1}H NMR (499 MHz, CHLOROFORM-d) δ 7.93 (d, *J*=8.0 Hz, 1H), 7.11 (d, *J*=8.0 Hz, 1H), 7.05 (s, 1H), 2.91 (t, *J*=6.0 Hz, 2H), 2.62 (t, *J*=6.5 Hz, 2H), 2.37 (s, 3H), 2.11 (app quin, *J*=6.3 Hz, 2H); ^{13}C{^{1}H} NMR (126 MHz, CHLOROFORM-d) δ 198.3, 144.7, 144.3, 130.5, 129.3, 127.8, 127.4, 39.3, 29.8, 23.5, 21.8; HRMS (ESI) *m/z* calcd for $C_{11}H_{13}O$ [M+H$^+$] 161.0961, found 161.0962.



11b

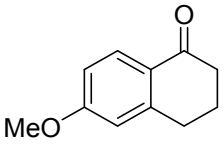
6-phenyl-3,4-dihydronaphthalen-1(2*H*)-one (11b). Cyclization product prepared by the general procedure for one-pot NAP formation and intramolecular arene alkylation using 5-([1,1'-biphenyl]-4-yl)-5-oxopentanoic acid (134 mg, 0.5

mmol, 1 equiv), *N*-hydroxyphthalimide (106 mg, 0.65 mmol, 1.3 equiv), DMAP (3 mg, 0.025 mmol, 0.05 equiv), DIC (0.12 mL, 0.75 mmol, 1.5 equiv), and DMSO (2.5 mL) stirring for 16.5 h for NAP formation then telescoping into photochemistry using 4CzIPN (**PC1**, 2 mg, 2.5 µmol, 0.5 mol %) and TFA (0.38 mL, 5.0 mmol, 10 equiv), diluting with DMSO (22.5 mL), and irradiating with purple light for 7 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 6-phenyl-3,4-dihydronaphthalen-1(2*H*)-one (**11b**, 69 mg, 62% yield) as an off-white solid. LCMS t_r = 1.03 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 8.11 (d, *J*=8.1 Hz, 1H), 7.65 - 7.59 (m, 2H), 7.54 (dd, *J*=8.1, 1.7 Hz, 1H), 7.50 - 7.43 (m, 3H), 7.42 - 7.36 (m, 1H), 3.03 (t, *J*=6.0 Hz, 2H), 2.73 - 2.65 (m, 2H), 2.23 - 2.14 (m, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 198.2, 146.2, 145.1, 140.2, 131.6, 129.0, 128.3, 128.0, 127.4 (2 signals by HSQC), 125.7, 39.3, 30.1, 23.5; HRMS (ESI) *m/z* calcd for $C_{16}H_{15}O$ [M+H$^+$] 223.1117, found 223.1119.



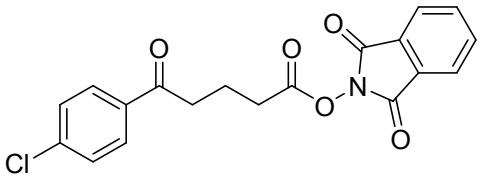
12a

1,3-dioxoisoindolin-2-yl 5-(4-methoxyphenyl)-5-oxopentanoate (12a). NAP prepared by the general procedure for NAP formation using 5-(4-methoxyphenyl)-5-oxopentanoic acid (805 mg, 3.62 mmol, 1 equiv), *N*-hydroxyphthalimide (808 mg, 4.95 mmol, 1.37 equiv), DMAP (18 mg, 0.15 mmol, 0.04 equiv), DIC (0.70 mL, 4.50 mmol, 1.24 equiv), and THF (15 mL) stirring for 25.5 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 5-(4-methoxyphenyl)-5-oxopentanoate (**12a**, 1.25 g, 94% yield) as a clear oil that solidified into a white solid on standing. LCMS t_r = 0.93 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.99 (d, *J*=8.9 Hz, 2H), 7.93 - 7.86 (m, 2H), 7.83 - 7.75 (m, 2H), 6.95 (d, *J*=9.0 Hz, 2H), 3.87 (s, 3H), 3.14 (t, *J*=7.1 Hz, 2H), 2.82 (t, *J*=7.0 Hz, 2H), 2.23 (quin, *J*=7.0 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 197.6, 169.6, 163.7, 162.1, 134.9, 130.5, 130.0, 129.1, 124.1, 113.9, 55.6, 36.5, 30.5, 19.5; HRMS (ESI) *m/z* calcd for $C_{20}H_{18}NO_6$ [M+H$^+$] 368.1129, found 368.1135.



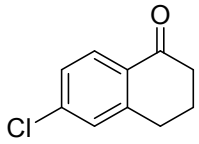
12b

6-methoxy-3,4-dihydronaphthalen-1(2*H*)-one (12b). Cyclization product prepared by the general procedure for intramolecular arene alkylation using **12a** (184 mg, 0.5 mmol, 1 equiv), 4CzIPN (**PC1**, 2 mg, 2.5 µmol, 0.5 mol %), and TFA (0.38 mL, 5.0 mmol, 10 equiv) in DMSO (25 mL) irradiating with purple light for 7 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 6-methoxy-3,4-dihydronaphthalen-1(2*H*)-one (**12b**, 57 mg, 65% yield) as a light yellow solid. LCMS t_r = 0.81 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 8.01 (d, *J*=8.8 Hz, 1H), 6.82 (dd, *J*=8.7, 2.5 Hz, 1H), 6.70 (d, *J*=2.3 Hz, 1H), 3.86 (s, 3H), 2.93 (t, *J*=6.1 Hz, 2H), 2.65 - 2.56 (m, 2H), 2.12 (app quin, *J*=6.3 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 197.3, 163.7, 147.1, 129.8, 126.5, 113.2, 112.8, 55.6, 39.1, 30.3, 23.5; HRMS (ESI) *m/z* calcd for $C_{11}H_{13}O_2$ [M+H$^+$] 177.0910, found 177.0912.



13a

1,3-dioxoisoindolin-2-yl 5-(4-chlorophenyl)-5-oxopentanoate (13a). NAP prepared by the general procedure for NAP formation using 5-(4-chlorophenyl)-5-oxopentanoic acid (2.0 g, 8.82 mmol, 1 equiv), *N*-hydroxyphthalimide (2.38 g, 14.6 mmol, 1.65 equiv), DMAP (54 mg, 0.441 mmol, 0.05 equiv), DIC (2.06 mL, 13.2 mmol, 1.5 equiv), and THF (44 mL) stirring for 67 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 5-(4-chlorophenyl)-5-oxopentanoate (**13a**, 2.44 g, 74% yield) as a white solid. LCMS t_r = 0.99 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.95 (app d, *J*=8.6 Hz, 2H), 7.92 - 7.86 (m, 2H), 7.83 - 7.76 (m, 2H), 7.45 (app d, *J*=8.6 Hz, 2H), 3.17 (t, *J*=7.1 Hz, 2H), 2.83 (t, *J*=6.9 Hz, 2H), 2.24 (quin, *J*=7.0 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 197.8, 169.5, 162.1, 139.8, 135.2, 135.0, 129.7, 129.1, 129.1, 124.2, 36.8, 30.4, 19.3; HRMS (ESI) *m/z* calcd for $C_{19}H_{15}NO_5Cl$ [M+H$^+$] 372.0633, found 372.0637.



13b

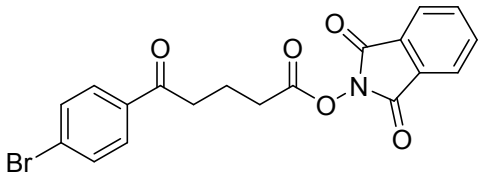
6-chloro-3,4-dihydronaphthalen-1(2*H*)-one (13b). Cyclization product prepared by the general procedure for intramolecular arene alkylation using **13a** (186 mg, 0.5 mmol, 1 equiv), 4CzIPN (**PC1**, 2 mg, 2.5 µmol, 0.5 mol %), and TFA (0.38 mL, 5.0 mmol, 10 equiv) in DMSO (25 mL) irradiating with purple light for 7 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 6-chloro-3,4-dihydronaphthalen-1(2*H*)-one (**13b**, 65 mg, 72% yield) as a yellow oil. See below for 2.0 mmol scale in batch and flow. LCMS t_r = 0.89 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.97 (d, *J*=8.2 Hz, 1H), 7.30 - 7.24 (m, 2H), 2.94 (t, *J*=6.1 Hz, 2H), 2.68 - 2.62 (m, 2H), 2.18 - 2.09 (m, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 197.3, 146.1, 139.8, 131.2, 129.0, 128.8, 127.3, 39.1, 29.7, 23.2; HRMS (ESI) *m/z* calcd for $C_{10}H_{10}OCl$ [M+H$^+$] 181.0415, found 181.0416.

Procedures for 6-chloro-3,4-dihydronaphthalen-1(2*H*)-one (13b) formed on 2.0 mmol scale. Procedure for 13b formed in batch: Cyclization product prepared by the general procedure for intramolecular arene alkylation in a 250 mL flask with a nitrogen balloon affixed using **13a** (744 mg, 2.0 mmol, 1 equiv), 4CzIPN (**PC1**, 8 mg, 10 µmol, 0.5 mol %), and TFA (1.53 mL, 20 mmol, 10 equiv) in DMSO (100 mL). The reaction was degassed with nitrogen gas for 5 minutes and then irradiated with purple light for 7 h by placing the flask between

two 40 W Kessil lamps model PR160 427 (purple light, λ_{max} = 427 nm) set to 100% and about 12 cm apart. An overhead cooling fan was used to keep the reaction at or near room temperature. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 6-chloro-3,4-dihydronaphthalen-1(2*H*)-one (**13b**, 242 mg, 67% yield) as a yellow oil. qNMR adjustment of yield by purity assessment using trimethoxybenzene as an internal standard gave 96.4% purity and a qNMR adjusted yield of 65%. Characterization details for **13b** can be found above.

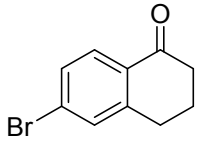
Procedure for 13b formed in flow. General flow chemistry comments: Flow chemistry experiments were carried out on a Vapourtec E-series reactor platform (Vapourtec Ltd, Bury St Edmunds, U.K.) equipped with a UV-150 photochemistry module. Please see the Vapourtec website for more information about the flow reactor and LED arrays. The reactor coil consisted of a 10 mL FEP tubular reactor within which an LED array (either 420 nm 18W or 440 nm 24W) was positioned. Reactor temperature was kept constant with heated air provided by the reactor. Reaction mixtures were degassed with N_2 sparge for up to 5 minutes before being loaded onto the reactor in automatic mode with a flow rate to match the desired residence time (eg. 0.143 mL/min for tR = 70 min). Only the steady state (as modeled by the reactor software) was collected for follow-up analysis by HPLC.

Procedure for 13b formed in flow: A conical 2-neck flask was charged with **13a** (800 mg, 2.15 mmol, 1 equiv), 4CzIPN (**PC1**, 42.9 mg, 0.054 mmol, 2.5 mol %), and DMSO (108 mL) and sonicated. TFA (1.63 mL, 21.6 mmol, 10 equiv) was added, and the reaction mixture was degassed with nitrogen gas bubbling. The reaction mixture was injected onto the Vapourtec reactor at 0.143 mL/min (tR = 70 min) with 420 nm LED irradiation. Total run time was 800 min with sample collection of 98 mL of the reaction mixture from 90 – 770 minutes at steady state (1.96 mmol for yield basis). The crude reaction mixture was worked up and purified as detailed in the general procedure for intramolecular arene alkylation. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 6-chloro-3,4-dihydronaphthalen-1(2*H*)-one (**13b**, 223 mg, 63% yield) as a yellow oil. qNMR adjustment of yield by purity assessment using trimethoxybenzene as an internal standard gave 89.9% purity and a qNMR adjusted yield of 57%.



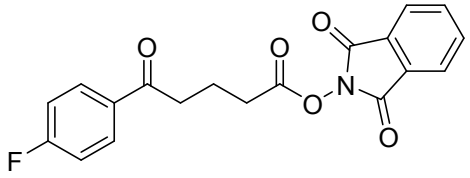
14a

1,3-dioxoisoindolin-2-yl 5-(4-bromophenyl)-5-oxopentanoate (14a). NAP prepared by the general procedure for NAP formation using 5-(4-bromophenyl)-5-oxopentanoic acid (542 mg, 2 mmol, 1 equiv), *N*-hydroxyphthalimide (538 mg, 3.3 mmol, 1.65 equiv), DMAP (12 mg, 0.1 mmol, 0.05 equiv), DIC (0.47 mL, 3 mmol, 1.5 equiv), and THF (10 mL) stirring for 21 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 5-(4-bromophenyl)-5-oxopentanoate (**14a**, 468 mg, 56% yield) as a shiny white solid. LCMS t_r = 1.01 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.93 - 7.85 (m, 4H), 7.83 - 7.77 (m, 2H), 7.65 - 7.59 (m, 2H), 3.17 (t, *J*=7.1 Hz, 2H), 2.82 (t, *J*=6.9 Hz, 2H), 2.23 (quin, *J*=7.0 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 198.0, 169.5, 162.1, 135.6, 135.0, 132.1, 129.8, 129.1, 128.6, 124.2, 36.8, 30.3, 19.3; HRMS (ESI) *m/z* calcd for $C_{19}H_{15}NO_5Br$ [M+H$^+$] 416.0128, found 416.0135 and 418.0113 [(M+2)+H$^+$].



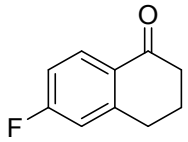
14b

6-bromo-3,4-dihydronaphthalen-1(2*H*)-one (14b). Cyclization product prepared by the general procedure for intramolecular arene alkylation using **14a** (208 mg, 0.5 mmol, 1 equiv), 4CzIPN (**PC1**, 2 mg, 2.5 µmol, 0.5 mol %), and TFA (0.38 mL, 5.0 mmol, 10 equiv) in DMSO (25 mL) irradiating with purple light for 7 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 6-bromo-3,4-dihydronaphthalen-1(2*H*)-one (**14b**, 75 mg, 67% yield) as a yellow oil. LCMS t_r = 0.95 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.92 - 7.85 (m, 1H), 7.46 - 7.41 (m, 2H), 2.94 (t, *J*=6.1 Hz, 2H), 2.67 - 2.61 (m, 2H), 2.18 - 2.09 (m, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 197.5, 146.3, 131.8, 131.6, 130.3, 129.1, 128.7, 39.1, 29.6, 23.2; HRMS could not be obtained for this material; sample would not ionize under HRMS conditions. Low resolution MS observed 225.1/227.3 [M+H$^+$]/[(M+2)+H$^+$].



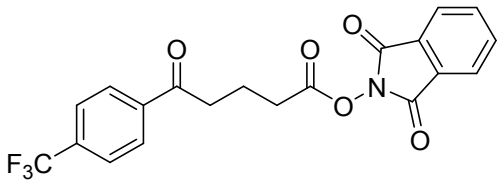
15a

1,3-dioxoisoindolin-2-yl 5-(4-fluorophenyl)-5-oxopentanoate (15a). NAP prepared by the general procedure for NAP formation using 5-(4-fluorophenyl)-5-oxopentanoic acid (420 mg, 2 mmol, 1 equiv), *N*-hydroxyphthalimide (538 mg, 3.3 mmol, 1.65 equiv), DMAP (12 mg, 0.1 mmol, 0.05 equiv), DIC (0.47 mL, 3 mmol, 1.5 equiv), and THF (10 mL) stirring for 22 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 5-(4-fluorophenyl)-5-oxopentanoate (**15a**, 665 mg, 94% yield) as a clear oil that solidified on standing into a white solid. LCMS t_r = 0.96 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 8.07 - 8.00 (m, 2H), 7.93 - 7.86 (m, 2H), 7.83 - 7.77 (m, 2H), 7.19 - 7.10 (m, 2H), 3.17 (t, *J*=7.1 Hz, 2H), 2.83 (t, *J*=6.9 Hz, 2H), 2.24 (quin, *J*=7.0 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 197.4, 169.5, 166.0 (d, *J*=254.6 Hz), 162.1, 134.9, 133.3 (d, *J*=2.9 Hz), 130.9 (d, *J*=9.5 Hz), 129.1, 124.2, 115.9 (d, *J*=22.0 Hz), 36.7, 30.4, 19.3; HRMS (ESI) *m/z* calcd for $C_{19}H_{15}NO_5F$ [M+H$^+$] 356.0929, found 356.0931.



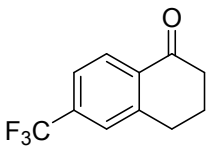
15b

6-fluoro-3,4-dihydronaphthalen-1(2*H*)-one (15b). Cyclization product prepared by the general procedure for intramolecular arene alkylation using **15a** (178 mg, 0.5 mmol, 1 equiv), 4CzIPN (**PC1**, 2 mg, 2.5 µmol, 0.5 mol %), and TFA (0.38 mL, 5.0 mmol, 10 equiv) in DMSO (25 mL) irradiating with purple light for 7 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 6-fluoro-3,4-dihydronaphthalen-1(2*H*)-one (**15b**, 43 mg, 52% yield) as a clear oil. LCMS t_r = 0.85 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 8.06 (dd, *J*=8.6, 6.1 Hz, 1H), 7.01 - 6.95 (m, 1H), 6.94 - 6.89 (m, 1H), 2.95 (t, *J*=6.1 Hz, 2H), 2.67 - 2.60 (m, 2H), 2.14 (app quin, *J*=6.3 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 196.9, 165.8 (d, *J*=255.3 Hz,), 147.6 (d, *J*=8.8 Hz), 130.4 (d, *J*=9.5 Hz), 129.4 (d, *J*=2.9 Hz), 115.2 (d, *J*=21.3 Hz), 114.4 (d, *J*=22.0 Hz), 39.0, 30.0 (d, *J*=1.5 Hz), 23.3; HRMS (ESI) *m/z* calcd for $C_{10}H_{10}OF$ [M+H$^+$] 165.0710, found 165.0713.



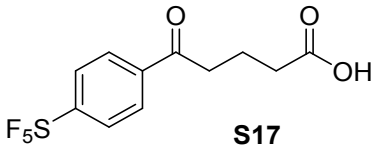
16a

1,3-dioxoisoindolin-2-yl 5-oxo-5-(4-(trifluoromethyl)phenyl)pentanoate (16a). NAP prepared by the general procedure for NAP formation using 5-oxo-5-(4-(trifluoromethyl)phenyl)pentanoic acid (520 mg, 2 mmol, 1 equiv), *N*-hydroxyphthalimide (538 mg, 3.3 mmol, 1.65 equiv), DMAP (12 mg, 0.1 mmol, 0.05 equiv), DIC (0.47 mL, 3 mmol, 1.5 equiv), and THF (10 mL) stirring for 17 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 5-oxo-5-(4-(trifluoromethyl)phenyl)pentanoate (**16a**, 678 mg, 84% yield) as a white solid. LCMS t_r = 1.01 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 8.12 (br d, *J*=8.1 Hz, 2H), 7.94 - 7.86 (m, 2H), 7.84 - 7.77 (m, 2H), 7.75 (br d, *J*=8.1 Hz, 2H), 3.24 (t, *J*=7.0 Hz, 2H), 2.84 (t, *J*=6.9 Hz, 2H), 2.26 (quin, *J*=7.0 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 198.0, 169.4, 162.1, 139.5 (app d, *J*=1.5 Hz), 135.0, 134.6 (q, *J*=32.8 Hz), 129.0, 128.6, 125.9 (q, *J*=3.7 Hz), 124.2, 123.7 (q, *J*=274 Hz), 37.1, 30.3, 19.2; HRMS (ESI) *m/z* calcd for $C_{20}H_{14}NO_5F_3Na$ [M+Na$^+$] 428.0716, found 428.0722.



16b

6-(trifluoromethyl)-3,4-dihydronaphthalen-1(2*H*)-one (16b). Cyclization product prepared by the general procedure for intramolecular arene alkylation using **16a** (203 mg, 0.5 mmol, 1 equiv), 4CzIPN (**PC1**, 2 mg, 2.5 µmol, 0.5 mol %), and TFA (0.38 mL, 5.0 mmol, 10 equiv) in DMSO (25 mL) irradiating with purple light for 24 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 6-(trifluoromethyl)-3,4-dihydronaphthalen-1(2*H*)-one (**16b**, 59 mg, 55% yield) as a clear oil. LCMS t_r = 0.96 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 8.13 (d, *J*=8.1 Hz, 1H), 7.59 - 7.49 (m, 2H), 3.03 (t, *J*=6.0 Hz, 2H), 2.74 - 2.66 (m, 2H), 2.23 - 2.14 (m, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 197.3, 145.0, 135.2 - 135.1 (m), 134.7 (q, *J*=32.3 Hz), 128.0, 126.1 (q, *J*=3.7 Hz, 1C), 123.5 (q, *J*=3.7 Hz, 1C), 123.7 (q, *J*=273 Hz), 39.1, 29.8, 23.1; HRMS (ESI) *m/z* calcd for $C_{11}H_{10}OF_3$ [M+H$^+$] 215.0678, found 215.0686.

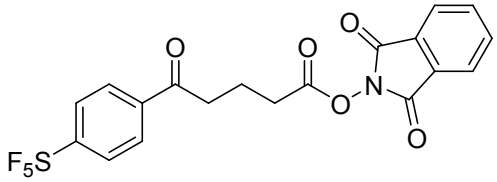


S17

5-oxo-5-(4-(pentafluoro-λ^6-sulfaneyl)phenyl)pentanoic acid (S17). 1-[bis(dimethylamino)methylene]-1*H*-1,2,3-triazolo[4,5-b]pyridinium 3-oxide hexafluorophosphate (HATU) (1.52 g, 3.99 mmol, 1.1 equiv) was added in one portion to a stirred solution of 4-(pentafluoro-λ^6-sulfaneyl)benzoic acid (900 mg, 3.63 mmol, 1.0 equiv), *N*,*O*-dimethylhydroxylamine hydrochloride (372 mg, 3.81 mmol, 1.05 equiv) and *N*,*N*-diisopropylethylamine (1.27 mL, 7.25 mmol, 2.0 equiv) in anhydrous DMF (6 mL) at room temperature. The reaction was stirred at room temperature for 10 min. The reaction was diluted with ethyl acetate, washed with saturated aqueous sodium bicarbonate solution and brine, dried over sodium sulfate, and concentrated. The crude material was purified by flash column chromatography using silica gel on a Teledyne Isco instrument to give *N*-methoxy-*N*-methyl-4-(pentafluoro-λ^6-sulfaneyl)benzamide (600 mg, 57% yield) as a clear oil. LCMS t_r = 0.87 min, *m/z* [M+H$^+$] 292.2. To a solution of *N*-methoxy-*N*-methyl-4-(pentafluoro-λ^6-sulfaneyl)benzamide (600 mg, 2.06 mmol, 1.0 equiv) in anhydrous THF (5 mL) was added a solution of pent-4-en-1-ylmagnesium bromide (0.5 M in THF, 8.24 mL, 4.12 mmol, 2.0 equiv) at 0 °C under a nitrogen atmosphere. The mixture was stirred at room temperature for 2 h. Saturated aqueous ammonium chloride solution (35 mL) was added. The mixture was diluted with EtOAc (35 mL) and the organic layer was separated, dried over sodium sulfate, and concentrated. The crude product was purified by flash column chromatography using silica gel on a Teledyne Isco instrument to give 1-(4-(pentafluoro-λ^6-sulfaneyl)phenyl)hex-5-en-1-one (520 mg, 84% yield) as a clear liquid. LCMS t_r = 1.10 min, m/z [M+H$^+$] 301.2. 1-(4-(pentafluoro-λ^6-sulfaneyl)phenyl)hex-5-en-1-one (420 mg, 1.40 mmol, 1.0 equiv) was dissolved in DCM (20 mL), acetonitrile (20 mL) and water (10 mL). $RuCl_3$ hydrate (31.5 mg, 0.140 mmol, 0.1 equiv) in water (10 mL) was added. After 5 min, $NaIO_4$ (1.50 g, 6.99 mmol, 5.0 equiv) was added. The reaction was stirred for 30 min. Upon completion, water (30 mL) and DCM (30 mL) were added. The organic layer was collected, dried over Na_2SO_4, and concentrated. The residue was purified by flash column chromatography using silica gel on a Teledyne Isco instrument to give 5-oxo-5-(4-(pentafluoro-λ^6-sulfaneyl)phenyl)pentanoic acid (**S17,** 290 mg, 65% yield) as a white solid. LCMS (with 0.01 M NH_4OAc buffer) t_r = 0.73 min, *m/z* [M–H$^+$] 316.9.

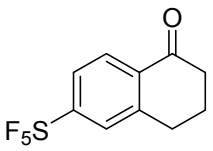
Alternative synthesis of S17: To a microwave vial was added 2-cyclopentenyl-4,4,5,5-tetramethyl-1,3,2-

dioxaborolane (411 mg, 2.12 mmol, 1.2 equiv), 1-bromo-4-(pentafluorosulfanyl)benzene (500 mg, 1.77 mmol, 1.0 equiv), an 8/1 mixture of 1,4-dioxane/EtOH (18 mL), aqueous potassium carbonate (2 M, 2.65 mL, 5.30 mmol, 3.0 equiv), and bis(triphenylphosphine)palladium(II) chloride (99 mg, 0.141 mmol, 0.08 equiv). The reaction mixture was purged with nitrogen and sealed. The reaction was then stirred at 130 °C in a Biotage Initiator microwave reactor for 30 min. The mixture was diluted with water (50 mL) and extracted with hexanes (20 mL, 2 x 10 mL). The hexanes extracts were dried over Na_2SO_4 and filtered through a pad of silica gel that was then rinsed with DCM. The filtrates were concentrated under reduced pressure to give a crude orange liquid in recovery considered to be quantitative (4-(cyclopent-1-en-1-yl)phenyl)pentafluoro-λ⁶-sulfane. The material was used as such in the next step. LC t_r = 1.49 min. (4-(cyclopent-1-en-1-yl)phenyl)pentafluoro-λ⁶-sulfane (1.76 mmol, 1.0 equiv), toluene (0.94 mL), DCM (20 mL) and acetonitrile (20 mL) were mixed. $RuCl_3$ hydrate (40 mg, 0.176 mmol, 0.1 equiv) in water (20 mL) was added at 0 °C followed by $NaIO_4$ (1.13 g, 5.28 mmol, 3.0 equiv). The reaction was stirred at 0 °C for 1 h at which time more $NaIO_4$ (0.4 g, 2.10 mmol, 1.2 equiv) was added, and the reaction was stirred at room temperature for 2 h. Then, another aliquot of $NaIO_4$ (0.4 g, 2.10 mmol, 1.2 equiv) was added, and the reaction was stirred at room temperature for 2 h. Upon completion, water (30 mL) and DCM (30 mL) were added. The mixture was filtered through a pad of celite. The aqueous layer was separated and extracted with DCM (2 x 15 mL). The combined organic solutions were dried over sodium sulfate, filtered, and concentrated under reduced pressure. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 5-oxo-5-(4-(pentafluoro-λ⁶-sulfaneyl)phenyl)pentanoic acid (**S17**, 400 mg, 71% yield) as a yellow solid containing some co-eluting impurities. A portion (47 mg) of this material was purified by reverse phase preparative HPLC using the following conditions: Column: Luna 5µ 30 X 100 mm (AXIA); solvent A: 10% MeOH - 90% H_2O - 0.1% TFA; solvent B: 90% MeOH - 10% H_2O - 0.1% TFA; gradient from 30% B to 100% B over 9 min then 100% B for 5 min, flow rate 40 mL/min, detection by UV at 220 nm. Collection of fractions containing the desired product gave 5-oxo-5-(4-(pentafluoro-λ⁶-sulfaneyl)phenyl)pentanoic acid (**S17**, 35 mg). LCMS t_r = 0.88 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 9.59 (br s, 1H), 8.03 (d, *J*=8.6 Hz, 2H), 7.85 (d, *J*=8.9 Hz, 2H), 3.10 (t, *J*=7.1 Hz, 2H), 2.52 (t, *J*=7.1 Hz, 2H), 2.09 (quin, *J*=7.1 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 197.9, 179.3, 157.0 (quin, *J*=17.8 Hz), 138.9, 128.6, 126.6 (quin, *J*=4.8 Hz), 37.8, 33.0, 18.9; HRMS (ESI) *m/z* calcd for $C_{11}H_{10}O_3F_5S$ [M–H$^+$] 317.0265, found 317.0276.



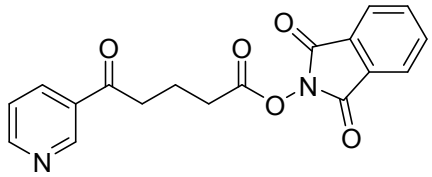
17a

1,3-dioxoisoindolin-2-yl 5-oxo-5-(4-(pentafluoro-λ⁶-sulfaneyl)phenyl)pentanoate (17a). NAP prepared by the general procedure for NAP formation using **S17c** (200 mg, 0.628 mmol, 1 equiv), *N*-hydroxyphthalimide (123 mg, 0.754 mmol, 1.2 equiv), DMAP (7.7 mg, 0.063 mmol, 0.1 equiv), DIC (0.29 mL, 1.89 mmol, 3 equiv), and DCM (3.1 mL) stirring for 20 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 5-oxo-5-(4-(pentafluoro-λ⁶-sulfaneyl)phenyl)pentanoate (**17a**, 200 mg, 69% yield) as a white solid. LCMS t_r = 1.06 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 8.09 (d, *J*=8.7 Hz, 2H), 7.92 - 7.84 (m, 4H), 7.83 - 7.76 (m, 2H), 3.23 (t, *J*=7.1 Hz, 2H), 2.83 (t, *J*=6.9 Hz, 2H), 2.25 (quin, *J*=7.0 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 197.5, 169.4, 162.1, 157.0 (quin, *J*=17.8 Hz), 138.9, 135.0, 129.0, 128.6, 126.6 (quin, *J*=4.7 Hz), 124.2, 37.1, 30.2, 19.1; HRMS (ESI) *m/z* calcd for $C_{19}H_{15}NO_5F_5S$ [M+H$^+$] 464.0586, found 464.0587.



17b

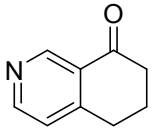
6-(pentafluoro-λ⁶-sulfaneyl)-3,4-dihydronaphthalen-1(2*H*)-one (17b). Cyclization product prepared by the general procedure for intramolecular arene alkylation using **17a** (260 mg, 0.488 mmol, 1 equiv), 4CzIPN (**PC1**, 1.9 mg, 2.44 µmol, 0.5 mol %), and TFA (0.43 mL, 5.61 mmol, 11.5 equiv) in DMSO (24.4 mL) irradiating with purple light for 7 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 6-(pentafluoro-λ⁶-sulfaneyl)-3,4-dihydronaphthalen-1(2*H*)-one (**17b**, 50 mg, 38% yield) as a clear yellowish liquid that solidified on standing. LCMS t_r = 0.99 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 8.09 (d, *J*=9.1 Hz, 1H), 7.69 - 7.64 (m, 2H), 3.03 (t, *J*=6.1 Hz, 2H), 2.73 - 2.65 (m, 2H), 2.23 - 2.14 (m, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 196.8, 157.0 (quin, *J*=17.4 Hz), 145.2, 134.6, 128.1, 126.6 (quin, *J*=4.6 Hz), 124.3 (quin, *J*=4.8 Hz), 39.0, 30.0, 23.1; HRMS could not be obtained for this material; sample would not ionize under HRMS conditions. Low resolution MS observed 273.1 [M+H$^+$].



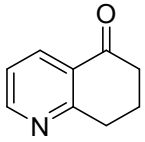
18a

1,3-dioxoisoindolin-2-yl 5-oxo-5-(pyridin-3-yl)pentanoate (18a). NAP prepared by the general procedure for NAP formation using 5-oxo-5-(pyridin-3-yl)pentanoic acid (483 mg, 2.5 mmol, 1 equiv), *N*-hydroxyphthalimide (673 mg, 4.13 mmol, 1.65 equiv), DMAP (15 mg, 0.13 mmol, 0.05 equiv), DIC (0.58 mL, 3.75 mmol, 1.5 equiv), and THF (12.5 mL) stirring for 29 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 5-oxo-5-(pyridin-3-yl)pentanoate (**18a**, 711 mg, 84% yield) as a white solid. LCMS t_r = 0.71 min; ^{1}H NMR (499 MHz, CHLOROFORM-d) δ 9.23 (dd, *J*=2.2, 0.8 Hz, 1H), 8.79 (dd, *J*=4.8, 1.7 Hz, 1H), 8.27 (app dt, *J*=8.0, 1.9 Hz, 1H), 7.91 - 7.87 (m, 2H), 7.82 - 7.77 (m, 2H), 7.43 (ddd, *J*=8.0, 4.9, 0.8 Hz, 1H), 3.23 (t, *J*=7.1 Hz, 2H), 2.84 (t, *J*=6.9 Hz, 2H), 2.26 (quin, *J*=7.0 Hz, 2H); ^{13}C{^{1}H} NMR (126 MHz, CHLOROFORM-d) δ 197.9, 169.4, 162.1, 153.8, 149.8, 135.5,

135.0, 132.1, 129.0, 124.2, 123.8, 37.1, 30.3, 19.0; HRMS (ESI) *m/z* calcd for $C_{18}H_{15}N_2O_5$ [M+H$^+$] 339.0975, found 339.0971.

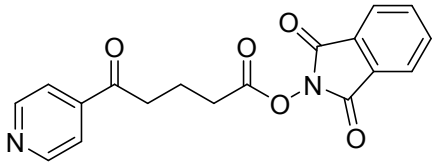


18ba



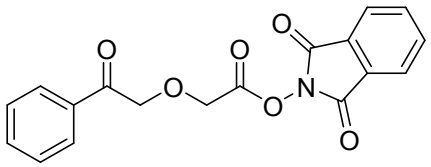
18bb

6,7-dihydroisoquinolin-8(5*H*)-one (18ba) and 7,8-dihydroquinolin-5(6*H*)-one (18bb). Cyclization products prepared by the general procedure for intramolecular arene alkylation using **18a** (169 mg, 0.5 mmol, 1 equiv), 4CzIPN (**PC1**, 2 mg, 2.5 µmol, 0.5 mol %), and TFA (0.38 mL, 5.0 mmol, 10 equiv) in DMSO (25 mL) irradiating with purple light for 5 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 6,7-dihydroisoquinolin-8(5*H*)-one (**18ba**) and 7,8-dihydroquinolin-5(6*H*)-one (**18bb**) as a 1.1:1 mixture of **18ba:18bb** (40 mg, 54% yield) as a light yellow oil. LCMS t_r = 0.40 min, 0.41 min (isomers unassigned); Major isomer **18ba**: ^{1}H NMR (499 MHz, CHLOROFORM-d) δ 9.14 (s, 1H), 8.60 (d, *J*=5.2 Hz, 1H), 7.17 (app dd, *J*=5.1, 0.7 Hz, 1H), 2.95 (t, *J*=6.2 Hz, 2H), 2.69 - 2.66 (m, 2H), 2.19 - 2.13 (m, 2H); Minor isomer **18bb**: ^{1}H NMR (499 MHz, CHLOROFORM-d) δ 8.66 (dd, *J*=4.8, 1.9 Hz, 1H), 8.26 (dd, *J*=7.9, 1.9 Hz, 1H), 7.30 - 7.25 (m, 1H), 3.15 (t, *J*=6.3 Hz, 2H), 2.71 - 2.68 (m, 2H), 2.23 - 2.17 (m, 2H); Carbon NMR peaks were not assigned to individual isomers: ^{13}C{^{1}H} NMR (126 MHz, CHLOROFORM-d) δ 198.1, 197.5, 163.8, 153.6, 153.1, 152.5, 149.5, 135.1, 128.3, 128.0, 123.5, 122.4, 39.2, 38.7, 32.7, 29.0, 22.6, 22.0; HRMS (ESI) *m/z* calcd for $C_9H_{10}NO$ [M+H$^+$] 148.0757, found 148.0755.



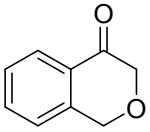
19a

1,3-dioxoisoindolin-2-yl 5-oxo-5-(pyridin-4-yl)pentanoate (19a). NAP prepared by the general procedure for NAP formation using 5-oxo-5-(pyridin-4-yl)pentanoic acid (580 mg, 3 mmol, 1 equiv), *N*-hydroxyphthalimide (808 mg, 4.95 mmol, 1.65 equiv), DMAP (18 mg, 0.15 mmol, 0.05 equiv), DIC (0.70 mL, 4.5 mmol, 1.5 equiv), and THF (15 mL) stirring for 24 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 5-oxo-5-(pyridin-4-yl)pentanoate (**19a**, 679 mg, 67% yield) as a white solid. LCMS t_r = 0.71 min; ^{1}H NMR (499 MHz, CHLOROFORM-d) δ 8.84 - 8.81 (m, 2H), 7.92 - 7.87 (m, 2H), 7.82 - 7.76 (m, 4H), 3.22 (t, *J*=7.0 Hz, 2H), 2.84 (t, *J*=6.9 Hz, 2H), 2.25 (quin, *J*=7.0 Hz, 2H); ^{13}C{^{1}H} NMR (126 MHz, CHLOROFORM-d) δ 198.5, 169.4, 162.1, 151.2, 142.5, 135.0, 129.0, 124.2, 121.2, 37.1, 30.2, 19.0; HRMS (ESI) *m/z* calcd for $C_{18}H_{15}N_2O_5$ [M+H$^+$] 339.0975, found 339.0979.



20a

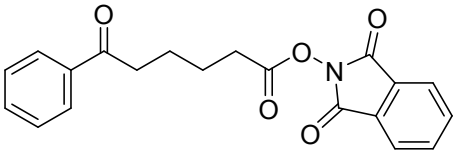
1,3-dioxoisoindolin-2-yl 2-(2-oxo-2-phenylethoxy)acetate (20a). To 1,4-dioxane-2,6-dione (998 mg, 8.60 mmol, 1.0 equiv) in benzene (17 mL, 191 mmol, 22.2 equiv) was added aluminum trichloride (3.36 g, 25.2 mmol, 2.93 equiv).[34] The reaction mixture was heated at 60-65 °C for two hours and then at reflux (80-85 °C) for one hour. Upon completion, the reaction was cooled to room temperature. Ice was added to the reaction mixture followed by 20 mL of concentrated HCl. This mixture was stirred for one hour and then extracted with EtOAc. The combined organics were washed with brine, dried over magnesium sulfate, filtered, and concentrated. Purification of the residue by silica gel chromatography provided a yellow-brown oil containing 2-(2-oxo-2-phenylethoxy)acetic acid (472 mg, 28% yield) as the major product. Despite the presence of some co-eluting impurities, this material was taken forward into next step as is and considered to be exclusively 2-(2-oxo-2-phenylethoxy)acetic acid for subsequent reagent calculations. LCMS t_r = 0.73 min, *m/z* [M+H$^+$] 194.9. **20a** prepared by the general procedure for NAP formation using 2-(2-oxo-2-phenylethoxy)acetic acid (472 mg, 2.43 mmol, 1 equiv), *N*-hydroxyphthalimide (654 mg, 4.01 mmol, 1.65 equiv), DMAP (15 mg, 0.12 mmol, 0.05 equiv), DIC (0.57 mL, 3.65 mmol, 1.5 equiv), and THF (12 mL) stirring for 22 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 2-(2-oxo-2-phenylethoxy)acetate (**20a**, 209 mg, 25% yield) as an oil that solidified into a beige solid, contained a small amount of a co-eluting impurity. LCMS t_r = 0.85 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.97 - 7.88 (m, 4H), 7.84 - 7.79 (m, 2H), 7.64 - 7.58 (m, 1H), 7.52 - 7.46 (m, 2H), 5.02 (s, 2H), 4.74 (s, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 194.9, 166.7, 161.7, 135.1, 134.6, 134.1, 129.0, 129.0, 128.0, 124.3, 73.6, 66.4; HRMS (ESI) *m/z* calcd for $C_{18}H_{14}NO_6$ [M+H$^+$] 340.0816, found 340.0810.



20b

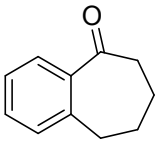
isochroman-4-one (20b). Cyclization product prepared by the general procedure for intramolecular arene alkylation using **20a** (85 mg, 0.25 mmol, 1 equiv), 4CzIPN (**PC1**, 1 mg, 1.3 µmol, 0.5 mol %), and TFA (0.19 mL, 2.5 mmol, 10 equiv) in DMSO (25 mL) irradiating with purple light for 23 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave isochroman-4-one (**20b**, 4 mg, 11% yield) as a clear oil containing a small amount of co-eluting impurities. LCMS t_r = 0.66 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 8.05 (d, *J*=8.0 Hz, 1H), 7.57 (td, *J*=7.5, 1.2 Hz, 1H), 7.42 (t, *J*=7.6 Hz, 1H), 7.23 (d, *J*=7.6 Hz, 1H), 4.90 (s, 2H), 4.38 (s, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 194.1, 141.9, 134.4, 129.7, 128.0, 126.6, 124.6, 73.7, 68.1; HRMS could not be obtained for this

material; sample would not ionize under HRMS conditions. Low resolution MS also could not be obtained on LCMS.



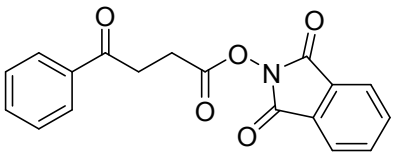
21a

1,3-dioxoisoindolin-2-yl 6-oxo-6-phenylhexanoate (21a). NAP prepared by the general procedure for NAP formation using 6-oxo-6-phenylhexanoic acid (619 mg, 3 mmol, 1 equiv), *N*-hydroxyphthalimide (808 mg, 4.95 mmol, 1.65 equiv), DMAP (18 mg, 0.15 mmol, 0.05 equiv), DIC (0.70 mL, 4.5 mmol, 1.5 equiv), and THF (15 mL) stirring for 21 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 6-oxo-6-phenylhexanoate (**21a**, 985 mg, 93% yield) as an off-white solid. LCMS t_r = 0.98 min; ^{1}H NMR (499 MHz, CHLOROFORM-d) δ 8.00 - 7.95 (m, 2H), 7.92 - 7.86 (m, 2H), 7.81 - 7.77 (m, 2H), 7.59 - 7.54 (m, 1H), 7.50 - 7.44 (m, 2H), 3.09 - 3.03 (m, 2H), 2.77 - 2.72 (m, 2H), 1.97 - 1.86 (m, 4H); ^{13}C{^{1}H} NMR (126 MHz, CHLOROFORM-d) δ 199.6, 169.5, 162.1, 137.0, 134.9, 133.2, 129.1, 128.8, 128.2, 124.1, 38.0, 31.1, 24.5, 23.4; HRMS (ESI) *m/z* calcd for $C_{20}H_{18}NO_5$ [M+H$^+$] 352.1179, found 352.1183.



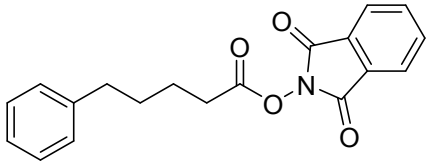
21b

6,7,8,9-tetrahydro-5*H*-benzo[7]annulen-5-one (21b). Cyclization product prepared by the general procedure for intramolecular arene alkylation using **21a** (176 mg, 0.5 mmol, 1 equiv), 4CzIPN (**PC1**, 2 mg, 2.5 μmol, 0.5 mol %), and TFA (0.38 mL, 5.0 mmol, 10 equiv) in DMSO (25 mL) irradiating with purple light for 7 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 6,7,8,9-tetrahydro-5*H*-benzo[7]annulen-5-one (**21b**, 11 mg, 14% yield) as a light yellow oil. Following the same procedure but irradiating with blue light for 7 h instead of purple light gave 6,7,8,9-tetrahydro-5*H*-benzo[7]annulen-5-one (**21b**, 12 mg, 15% yield) as a yellow oil. LCMS t_r = 0.88 min; ^{1}H NMR (499 MHz, CHLOROFORM-d) δ 7.72 (dd, *J*=7.7, 1.3 Hz, 1H), 7.42 (td, *J*=7.5, 1.4 Hz, 1H), 7.30 (td, *J*=7.5, 1.1 Hz, 1H), 7.22 - 7.18 (m, 1H), 2.96 - 2.91 (m, 2H), 2.76 - 2.71 (m, 2H), 1.92 - 1.85 (m, 2H), 1.85 - 1.78 (m, 2H); ^{13}C{^{1}H} NMR (126 MHz, CHLOROFORM-d) δ 206.3, 141.4, 139.0, 132.3, 129.8, 128.7, 126.8, 41.0, 32.7, 25.4, 21.1; HRMS (ESI) *m/z* calcd for $C_{11}H_{13}O$ [M+H$^+$] 161.0961, found 161.0963.



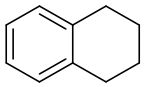
22a

1,3-dioxoisoindolin-2-yl 4-oxo-4-phenylbutanoate (22a). NAP prepared by the general procedure for NAP formation using 4-oxo-4-phenylbutanoic acid (535 mg, 3 mmol, 1 equiv), *N*-hydroxyphthalimide (808 mg, 4.95 mmol, 1.65 equiv), DMAP (18 mg, 0.15 mmol, 0.05 equiv), DIC (0.70 mL, 4.5 mmol, 1.5 equiv), and THF (15 mL) stirring for 21.5 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 4-oxo-4-phenylbutanoate (**22a**, 756 mg, 78% yield) as a yellow solid. LCMS t_r = 0.93 min; ^{1}H NMR (499 MHz, CHLOROFORM-d) δ 8.03 - 7.99 (m, 2H), 7.92 - 7.87 (m, 2H), 7.82 - 7.76 (m, 2H), 7.61 - 7.56 (m, 1H), 7.51 - 7.46 (m, 2H), 3.51 - 3.45 (m, 2H), 3.16 (t, *J*=6.9 Hz, 2H); ^{13}C{^{1}H} NMR (126 MHz, CHLOROFORM-d) δ 196.6, 169.5, 162.0, 136.3, 134.9, 133.6, 129.1, 128.9, 128.3, 124.1, 33.4, 25.6; HRMS (ESI) *m/z* calcd for $C_{18}H_{14}NO_5$ [M+H$^+$] 324.0866, found 324.0869.



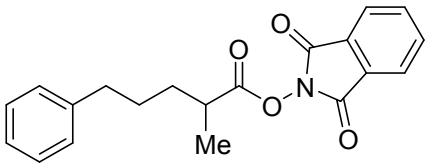
23a

1,3-dioxoisoindolin-2-yl 5-phenylpentanoate (23a). NAP prepared by the general procedure for NAP formation using 5-phenylvaleric acid (1 g, 5.61 mmol, 1 equiv), *N*-hydroxyphthalimide (1.01 g, 6.17 mmol, 1.1 equiv), DMAP (34 mg, 0.28 mmol, 0.05 equiv), DIC (1.31 mL, 8.42 mmol, 1.5 equiv), and DCM (10 mL) with reagents mixed at 0 °C then warmed to room temperature with reaction stirring for 18 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 5-phenylpentanoate (**23a**, 1.81 g, 100% yield) as a white solid. LC t_r = 1.34 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.92 - 7.85 (m, 2H), 7.83 - 7.75 (m, 2H), 7.34 - 7.27 (m, 2H), 7.25 - 7.15 (m, 3H), 2.75 - 2.64 (m, 4H), 1.90 - 1.74 (m, 4H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 169.6, 162.1, 141.8, 134.9, 129.1, 128.5, 128.5, 126.0, 124.1, 35.5, 31.0, 30.6, 24.4; HRMS (ESI) *m/z* calcd for $C_{19}H_{18}NO_4$ [M+H$^+$] 324.1230, found 324.1232.



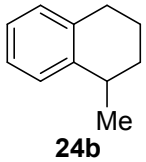
23b

tetralin (23b). Cyclization product prepared by the general procedure for intramolecular arene alkylation using **23a** (162 mg, 0.5 mmol, 1 equiv), 4CzIPN (**PC1**, 2 mg, 2.5 μmol, 0.5 mol %), and TFA (0.38 mL, 5.0 mmol, 10 equiv) in DMSO (25 mL) irradiating with purple light for 24 h. Due to difficulties in purification, an NMR yield of tetralin (**23b**) in the crude reaction mixture was obtained using CH_2Br_2 as an internal standard giving 70% NMR yield. For characterization purposes, the crude material was purified by flash column chromatography using silica gel on a Teledyne Isco instrument to give tetralin (**23b**, 40 mg) as a yellow oil containing small amounts of co-eluting impurities. HPLC column 1 t_r = 11.4 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.16 - 7.08 (m, 4H), 2.88 - 2.76 (m, 4H), 1.91 - 1.80 (m, 4H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 137.2, 129.3, 125.5, 29.5, 23.4; HRMS could not be obtained for this material; sample would not ionize under HRMS conditions. Low resolution MS also could not be obtained on LCMS.



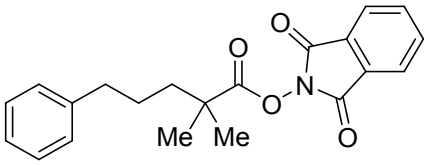
24a

1,3-dioxoisoindolin-2-yl 2-methyl-5-phenylpentanoate (24a). NAP prepared by the general procedure for NAP formation using 2-methyl-5-phenylvaleric acid (101 mg, 0.525 mmol, 1 equiv), *N*-hydroxyphthalimide (94 mg, 0.578 mmol, 1.1 equiv), DMAP (3.2 mg, 0.026 mmol, 0.05 equiv), DIC (0.12 mL, 0.788 mmol, 1.5 equiv), and DCM (1.5 mL) with reagents mixed at 0 °C then warmed to room temperature with reaction stirring for 3 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 2-methyl-5-phenylpentanoate (**24a**, 152 mg, 86% yield) as a colorless liquid. LC t_r = 1.39 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.91 - 7.85 (m, 2H), 7.81 - 7.74 (m, 2H), 7.33 - 7.28 (m, 2H), 7.26 - 7.17 (m, 3H), 2.93 - 2.82 (m, 1H), 2.70 (t, *J*=7.4 Hz, 2H), 1.95 - 1.75 (m, 3H), 1.74 - 1.63 (m, 1H), 1.36 (d, *J*=6.9 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 172.7, 162.1, 141.9, 134.8, 129.1, 128.5, 128.4, 125.9, 124.0, 37.1, 35.7, 33.3, 28.6, 17.1; HRMS (ESI) *m/z* calcd for $C_{20}H_{23}N_2O_4$ [M+NH_4^+] 355.1652, found 355.1653.



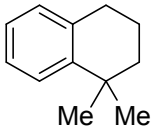
24b

1-methyl-1,2,3,4-tetrahydronaphthalene (24b). Cyclization product prepared by the general procedure for intramolecular arene alkylation using **24a** (150 mg, 0.445 mmol, 1 equiv), 4CzIPN (**PC1**, 1.8 mg, 2.2 µmol, 0.5 mol %), and TFA (0.34 mL, 4.45 mmol, 10 equiv) in DMSO (22.2 mL) irradiating with purple light for 24 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1-methyl-1,2,3,4-tetrahydronaphthalene (**24b**, 46 mg, 71% yield) as a clear, colorless liquid containing small amounts of co-eluting impurities. HPLC column 2 t_r = 10.1 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.27 - 7.07 (m, 4H), 2.96 (app dq, *J*=13.0, 6.6 Hz, 1H), 2.88 - 2.73 (m, 2H), 2.02 - 1.87 (m, 2H), 1.83 - 1.72 (m, 1H), 1.63 - 1.53 (m, 1H), 1.34 (d, *J*=7.0 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 142.3, 137.0, 129.1, 128.2, 125.7, 125.5, 32.6, 31.6, 30.1, 23.0, 20.6; HRMS (ESI) *m/z* calcd for $C_{11}H_{15}$ [M+H^+] 147.1168, found 147.1164.



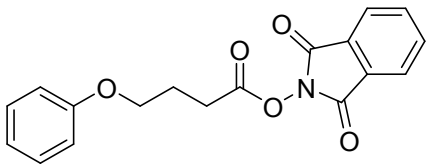
25a

1,3-dioxoisoindolin-2-yl 2,2-dimethyl-5-phenylpentanoate (25a). NAP prepared by the general procedure for NAP formation using 2,2-dimethyl-5-phenylvaleric acid (103 mg, 0.499 mmol, 1 equiv), *N*-hydroxyphthalimide (90 mg, 0.549 mmol, 1.1 equiv), DMAP (3.1 mg, 0.025 mmol, 0.05 equiv), DIC (0.12 mL, 0.749 mmol, 1.5 equiv), and DCM (1.5 mL) with reagents mixed at 0 °C then warmed to room temp with reaction stirring for 3 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 2,2-dimethyl-5-phenylpentanoate (**25a**, 158 mg, 90% yield) as a white solid. LC t_r = 1.43 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.91 - 7.85 (m, 2H), 7.80 - 7.74 (m, 2H), 7.34 - 7.25 (m, 4H), 7.23 - 7.18 (m, 1H), 2.74 - 2.67 (m, 2H), 1.88 - 1.75 (m, 4H), 1.40 (s, 6H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 173.9, 162.1, 142.0, 134.7, 129.1, 128.5, 128.4, 125.9, 123.9, 42.2, 40.3, 36.2, 26.5, 25.2; HRMS (ESI) *m/z* calcd for $C_{21}H_{20}NO_4$ [M–H^+] 350.1398, found 350.1400.



25b

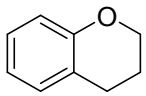
1,1-dimethyl-1,2,3,4-tetrahydronaphthalene (25b). Cyclization product prepared by the general procedure for intramolecular arene alkylation using **25a** (155 mg, 0.441 mmol, 1 equiv), 4CzIPN (**PC1**, 1.7 mg, 2.2 µmol, 0.5 mol %), and TFA (0.34 mL, 4.41 mmol, 10 equiv) in DMSO (22.1 mL) irradiating with purple light for 24 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,1-dimethyl-1,2,3,4-tetrahydronaphthalene (**25b**, 38 mg, 54% yield) as a clear, colorless liquid containing small amounts of co-eluting impurities. An additional 14 mg of impure **25b** was obtained with co-eluting non-polar impurities that could not be removed; this material was not included in the calculation of yield. HPLC column 1 t_r = 12.6 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.37 (app d, *J*=7.7 Hz, 1H), 7.21 - 7.15 (m, 1H), 7.14 - 7.05 (m, 2H), 2.81 (t, *J*=6.3 Hz, 2H), 1.89 - 1.81 (m, 2H), 1.74 - 1.69 (m, 2H), 1.33 (s, 6H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 145.9, 136.2, 129.2, 126.8, 125.9, 125.4, 39.5, 34.0, 32.0, 30.9, 19.9; HRMS (ESI) *m/z* calcd for $C_{12}H_{17}$ [M+H^+] 161.1325, found 161.1328.



26a

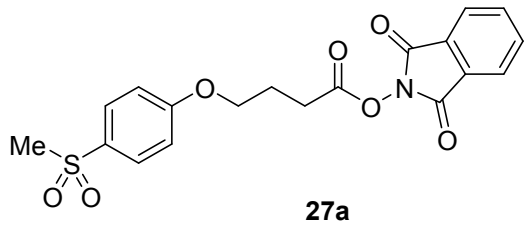
1,3-dioxoisoindolin-2-yl 4-phenoxybutanoate (26a). NAP prepared by the general procedure for NAP formation using 4-phenoxybutyric acid (500 mg, 2.77 mmol, 1 equiv), *N*-hydroxyphthalimide (453 mg, 2.77 mmol, 1 equiv), DMAP (17 mg, 0.14 mmol, 0.05 equiv), DIC (0.65 mL, 4.16 mmol, 1.5 equiv), and DCM (5 mL) with reagents mixed at 0 °C then warmed to room temp with reaction stirring for 16 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 4-phenoxybutanoate (**26a**, 780 mg, 86% yield) as a white solid. LC t_r = 1.25 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.93 - 7.86 (m, 2H), 7.83 - 7.76 (m, 2H), 7.33 - 7.27 (m, 2H), 6.99 - 6.90 (m, 3H), 4.10 (t, *J*=6.0 Hz, 2H), 2.92 (t, *J*=7.4 Hz, 2H), 2.32 - 2.23 (m, 1H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 169.5, 162.1, 158.8, 134.9, 129.6, 129.1,

124.1, 121.1, 114.7, 66.0, 28.0, 24.7; HRMS (ESI) *m/z* calcd for $C_{18}H_{16}NO_5$ [M+H$^+$] 326.1023, found 326.1023.



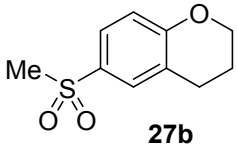
26b

chromane (26b). Cyclization product prepared by the general procedure for intramolecular arene alkylation using **26a** (163 mg, 0.5 mmol, 1 equiv), 4CzIPN (**PC1**, 2 mg, 2.5 µmol, 0.5 mol %), and TFA (0.38 mL, 5.0 mmol, 10 equiv) in DMSO (25 mL) irradiating with purple light for 24 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave chromane (**26b**, 16 mg, 24% yield) as a clear colorless liquid. HPLC column 1 t_r = 8.69 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.12 - 7.06 (m, 1H), 7.04 (d, *J*=7.5 Hz, 1H), 6.83 (td, *J*=7.4, 1.1 Hz, 1H), 6.80 (d, *J*=8.1 Hz, 1H), 4.22 - 4.16 (m, 2H), 2.80 (t, *J*=6.5 Hz, 2H), 2.06 - 1.97 (m, 2H) ; ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 155.0, 129.9, 127.3, 122.4, 120.2, 116.8, 66.6, 25.0, 22.5; HRMS could not be obtained for this material; sample would not ionize under HRMS conditions. Low resolution MS also could not be obtained on LCMS.



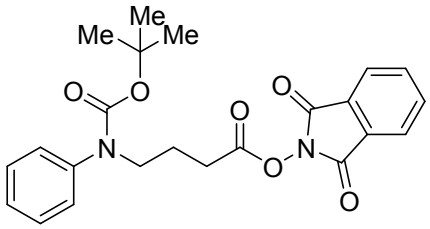
27a

1,3-dioxoisoindolin-2-yl 4-(4-(methylsulfonyl)phenoxy)butanoate (27a). NAP prepared by the general procedure for NAP formation using 4-(4-(methylsulfonyl)phenoxy)butanoic acid (258 mg, 1 mmol, 1 equiv), *N*-hydroxyphthalimide (269 mg, 1.65 mmol, 1.65 equiv), DMAP (6 mg, 0.05 mmol, 0.05 equiv), DIC (0.23 mL, 1.5 mmol, 1.5 equiv), and THF (5 mL) stirring for 18 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 4-(4-(methylsulfonyl)phenoxy)butanoate (**27a**, 378 mg, 94% yield) as a clear oil that solidified into a white solid on standing. LCMS t_r = 0.84 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.93 - 7.85 (m, 4H), 7.84 - 7.77 (m, 2H), 7.09 - 7.03 (m, 2H), 4.19 (t, *J*=6.0 Hz, 2H), 3.03 (s, 3H), 2.92 (t, *J*=7.1 Hz, 2H), 2.31 (quin, *J*=6.6 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 169.2, 162.9, 162.0, 135.0, 132.7, 129.8, 129.0, 124.2, 115.2, 66.6, 45.0, 27.8, 24.4; HRMS (ESI) *m/z* calcd for $C_{19}H_{18}NO_7S$ [M+H$^+$] 404.0798, found 404.0806.



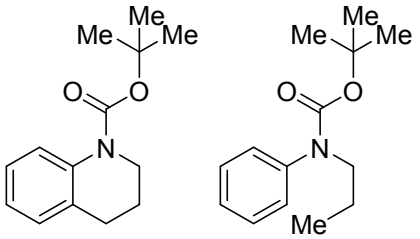
27b

6-(methylsulfonyl)chromane (27b). Cyclization product prepared by the general procedure for intramolecular arene alkylation using **27a** (202 mg, 0.5 mmol, 1 equiv), 4CzIPN (**PC1**, 2 mg, 2.5 µmol, 0.5 mol %), and TFA (0.38 mL, 5.0 mmol, 10 equiv) in DMSO (25 mL) irradiating with purple light for 24 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 6-(methylsulfonyl)chromane (**27b**, 24 mg, 23% yield) as a clear oil. HPLC column 1 t_r = 5.84 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.66 - 7.60 (m, 2H), 6.93 - 6.88 (m, 1H), 4.30 - 4.23 (m, 2H), 3.02 (s, 3H), 2.85 (t, *J*=6.4 Hz, 2H), 2.09 - 2.00 (m, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 159.5, 131.7, 129.8, 127.0, 123.2, 117.8, 67.2, 45.0, 25.0, 21.8; HRMS (ESI) *m/z* calcd for $C_{10}H_{13}O_3S$ [M+H$^+$] 213.0580, found 213.0581.



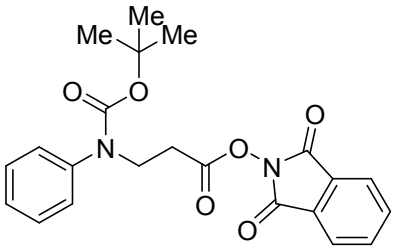
28a

1,3-dioxoisoindolin-2-yl 4-((*tert*-butoxycarbonyl)(phenyl)amino)butanoate (28a). 4-(phenylamino)butanoic acid hydrochloride (243 mg, 1.13 mmol, 1.0 equiv) was dissolved in water (2 mL) at room temperature and then 1,4-dioxane (2.8 mL) was added followed by Boc anhydride (0.26 mL, 1.14 mmol, 1.0 equiv).[35] Sodium bicarbonate (95 mg, 1.13 mmol, 1.0 equiv) dissolved in water (0.8 mL) was then immediately added at room temperature. The reaction was stirred for 18 h at room temperature, and then another aliquot of sodium bicarbonate (120 mg, 1.97 mmol, 1.75 equiv) was dissolved in water (2 mL) and added to the reaction. The reaction was then stirred for 45 min and then diluted with water (10 mL) and extracted with EtOAc (2x15 mL). The combined organic layer was set aside. Then the aqueous layer was adjusted to pH 1-2 as judged by pH paper by the addition of 1 M HCl and then quickly extracted with EtOAc (3x20 mL). The combined organic layer from the acidic extraction was dried over magnesium sulfate, filtered, and concentrated to provide 4-((*tert*-butoxycarbonyl)(phenyl)amino)butanoic acid (198 mg, 63% yield) as a brown oil. This material was carried forward into the next step as is. LCMS t_r = 0.86 min, *m/z* [M–*t*Bu+H$^+$] 224.1. **28a** prepared by the general procedure for NAP formation using 4-((*tert*-butoxycarbonyl)(phenyl)amino)butanoic acid (198 mg, 0.71 mmol, 1 equiv), *N*-hydroxyphthalimide (191 mg, 1.17 mmol, 1.65 equiv), DMAP (7 mg, 0.06 mmol, 0.08 equiv), DIC (0.17 mL, 1.06 mmol, 1.5 equiv), and THF (3.5 mL) stirring for 19 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 4-((*tert*-butoxycarbonyl)(phenyl)amino)butanoate (**28a**, 254 mg, 84% yield) as a clear oil that solidified on standing into white solid. LCMS t_r = 1.07 min; ^{1}H NMR (499 MHz, CHLOROFORM-d) δ 7.87 - 7.82 (m, 2H), 7.78 - 7.73 (m, 2H), 7.36 - 7.30 (m, 2H), 7.23 - 7.15 (m, 3H), 3.80 - 3.74 (m, 2H), 2.69 (t, *J*=7.6 Hz, 2H), 2.02 (app quin, *J*=7.4 Hz, 2H), 1.43 (br s, 9H); ^{13}C{^{1}H} NMR (126 MHz, CHLOROFORM-d) δ 169.1, 161.9, 154.8, 142.2, 134.8, 129.0, 128.9, 127.1, 126.3, 124.0, 80.5, 48.9, 28.5, 28.4, 23.7; HRMS (ESI) *m/z* calcd for $C_{23}H_{24}N_2O_6Na$ [M+Na$^+$] 447.1527, found 447.1515.



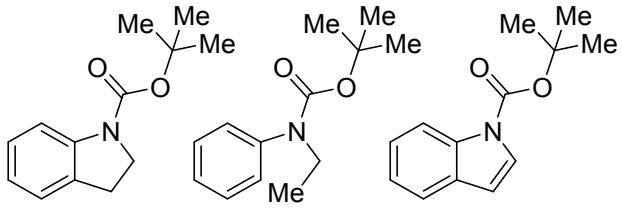
28b **28c**

***tert*-butyl 3,4-dihydroquinoline-1(2*H*)-carboxylate (28b).** Cyclization product prepared by the general procedure for intramolecular arene alkylation using **28a** (125 mg, 0.29 mmol, 1 equiv), 4CzIPN (**PC1**, 1.2 mg, 1.5 µmol, 0.5 mol %), and TFA (0.23 mL, 2.9 mmol, 10 equiv) in DMSO (14.7 mL) irradiating with purple light for 6 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave *tert*-butyl 3,4-dihydroquinoline-1(2*H*)-carboxylate (**28b**, 40 mg, 58% yield) as a clear oil of a 12.5:1 ratio of **28b** to uncyclized material **28c**. **28c** co-elutes with **28b**. LCMS t_r = 1.08 min; ^{1}H NMR (499 MHz, CHLOROFORM-d) δ 7.65 (d, *J*=8.2 Hz, 1H), 7.16 - 7.11 (m, 1H), 7.07 (app dd, *J*=7.5, 0.9 Hz, 1H), 6.98 (td, *J*=7.5, 1.2 Hz, 1H), 3.73 - 3.69 (m, 2H), 2.77 (t, *J*=6.6 Hz, 2H), 1.96 - 1.89 (m, 2H), 1.53 (s, 9H); ^{13}C{^{1}H} NMR (126 MHz, CHLOROFORM-d) δ 154.1, 138.8, 130.0, 128.6, 125.8, 124.3, 123.3, 80.8, 44.8, 28.5, 27.6, 23.7; HRMS (ESI) *m/z* calcd for $C_{10}H_{12}NO_2$ [M–*t*Bu+H$^+$] 178.0863, found 178.0862.



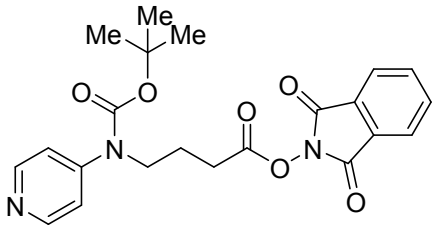
29a

1,3-dioxoisoindolin-2-yl 3-((*tert*-butoxycarbonyl)(phenyl)amino)propanoate (29a). 3-(phenylamino)propanoic acid (500 mg, 3.03 mmol, 1.0 equiv) was dissolved in 1,4-dioxane (5 mL). Sodium bicarbonate (254 mg, 3.03 mmol, 1.0 equiv) was dissolved in water (2.5 mL) and slowly added to the above solution. Then, Boc anhydride (0.70 mL, 3.06 mmol, 1.0 equiv) was added in a single portion at room temperature. The reaction was stirred for 21 h at room temperature. Upon completion, the reaction was diluted with water (10 mL), extracted with EtOAc (2x20 mL), and this organic layer was set aside. Then, the aqueous layer was adjusted to pH 1-2 as judged by pH paper with 1 M HCl and then quickly extracted with EtOAc (3x25 mL). The combined organic layer from the acidic extraction was dried over magnesium sulfate, filtered, and concentrated to provide 3-((*tert*-butoxycarbonyl)(phenyl)amino)propanoic acid (597 mg, 74% yield) as a cloudy, light purple oil. This material was carried forward into the next step as is. LCMS t_r = 0.84 min, *m/z* [M–*t*Bu+H$^+$] 210.4. **29a** prepared by the general procedure for NAP formation using 3-((*tert*-butoxycarbonyl)(phenyl)amino)propanoic acid (597 mg, 2.25 mmol, 1 equiv), *N*-hydroxyphthalimide (606 mg, 3.71 mmol, 1.65 equiv), DMAP (14 mg, 0.11 mmol, 0.05 equiv), DIC (0.53 mL, 3.38 mmol, 1.5 equiv), and THF (11.3 mL) stirring for 7.5 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 3-((*tert*-butoxycarbonyl)(phenyl)amino)propanoate (**29a**, 783 mg, 85% yield) as a light yellow oil that solidified into an off-white solid on standing. LCMS t_r = 1.05 min; ^{1}H NMR (499 MHz, CHLOROFORM-d) δ 7.90 - 7.85 (m, 2H), 7.81 - 7.76 (m, 2H), 7.40 - 7.34 (m, 2H), 7.27 - 7.18 (m, 3H), 4.10 - 4.05 (m, 2H), 3.02 - 2.97 (m, 2H), 1.44 (br s, 9H); ^{13}C{^{1}H} NMR (126 MHz, CHLOROFORM-d) δ 167.6, 161.9, 154.5, 141.9, 134.9, 129.2, 129.1, 127.3, 126.8, 124.1, 81.0 (br), 45.5, 30.5 (br), 28.4; HRMS (ESI) *m/z* calcd for $C_{22}H_{22}N_2O_6Na$ [M+Na$^+$] 433.1370, found 433.1362.



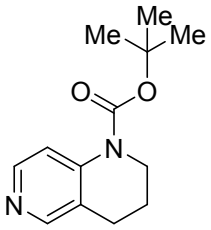
29b **29c** **29d**

***tert*-butyl indoline-1-carboxylate (29b).** Cyclization product prepared by the general procedure for intramolecular arene alkylation using **29a** (205 mg, 0.5 mmol, 1 equiv), 4CzIPN (**PC1**, 2 mg, 2.5 µmol, 0.5 mol %), and TFA (0.38 mL, 5.0 mmol, 10 equiv) in DMSO (25 mL) irradiating with purple light for 35 min. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave *tert*-butyl indoline-1-carboxylate (**29b**, 70 mg, 64% yield) as a light yellow oil in a 12.5:2.5:1 ratio of **29b:29c:29d** as all three compounds co-elute on silica gel. For characterization purposes, this material was purified by preparative SFC using the following conditions: Instrument: Berger SFC MGII; Column: Whelk-01 Column 31 X 250mm ID, 5 µm; Flow rate: 75.0 mL/min; Mobile Phase: 95/05 CO_2 / MeOH; Detector Wavelength: 215 nm; Sample Prep and Inj. Volume: 600 µL of ~6 mL sample (70 mg in 6 mL MeOH). The fractions containing the desired material were concentrated and repurified by flash column chromatography using silica gel on a Teledyne Isco instrument to obtain *tert*-butyl indoline-1-carboxylate (**29b**, 46 mg) for use in characterization. Characterization data for **29b** has been reported and matches data collected on our sample.[36] Characterization data for **29d** has been reported and was used to identify **29d** in the isolated mixture described above.[37] LCMS t_r = 1.07 min; ^{1}H NMR (499 MHz, CHLOROFORM-d) δ 8.07 - 7.32 (br m, 1H), 7.20 - 7.10 (m, 2H), 6.92 (td, *J*=7.5, 1.0 Hz, 1H), 3.97 (br t, *J*=7.7 Hz, 2H), 3.08 (t, *J*=8.7 Hz, 2H), 1.57 (br s, 9H); ^{13}C{^{1}H} NMR (126 MHz, CHLOROFORM-d) δ 152.7 (br); rotameric signals: 142.9 (br), 142.3 (br); rotameric signals: 131.7 (br), 131.0 (br); 127.5; 124.8 (br); 122.2; 114.8; rotameric signals: 81.4 (br), 80.5 (br); 47.7 (br), 28.6, 27.5 (br); HRMS (ESI) *m/z* calcd for $C_9H_{10}NO_2$ [M–*t*Bu+H$^+$] 164.0706, found 164.0705.



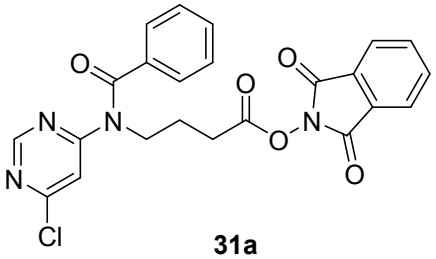
30a

1,3-dioxoisoindolin-2-yl 4-((*tert*-butoxycarbonyl)(pyridin-4-yl)amino)butanoate (30a). To a stirred solution of 4-(*tert*-butoxycarbonylamino)pyridine (0.5 g, 2.57 mmol, 1.0 equiv) in anhydrous DMF (2 mL) was added 60% mineral oil dispersion of NaH (0.15 g, 3.75 mmol, 1.46 equiv). The mixture was stirred for 30 min at room temperature before 5-bromo-1-pentene (0.46 mL, 3.86 mmol, 1.50 equiv) was added at room temperature with water bath cooling. The mixture was stirred for 16 h at room temperature. Upon completion, the reaction was quenched by the addition of saturated aqueous NH_4Cl solution (3 mL) and water (15 mL). The mixture was extracted with ethyl acetate (3x5 mL). The combined organic extracts were dried over sodium sulfate, filtered, and concentrated. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument afforded *tert*-butyl pent-4-en-1-yl(pyridin-4-yl)carbamate (318 mg, 47% yield) as a clear liquid. LCMS t_r = 0.72 min, *m/z* [M+H$^+$] 263.3. To a stirred mixture of *tert*-butyl pent-4-en-1-yl(pyridin-4-yl)carbamate (1.04 g, 3.96 mmol, 1.0 equiv), CCl_4 (5 mL), acetonitrile (5 mL), water (7.5 mL), and $NaIO_4$ (3.39 g, 15.9 mmol, 4.0 equiv) was added $RuCl_3$ hydrate (0.018 g, 0.079 mmol, 0.02 equiv) at room temperature with water bath cooling. The resulting solution was stirred for 16 h at room temperature. More $NaIO_4$ (0.5 g, 2.34 mmol, 0.59 equiv) was added. The mixture was stirred for 1 h at room temperature. DCM (40 mL) was added. The DCM layer was separated by decantation. The residual mixture was extracted with DCM (20 mL). The combined DCM extractions were concentrated. The residue was made basic with saturated aqueous sodium bicarbonate solution (20 mL) and washed with Et_2O (2 x 15 mL). The aqueous layer was acidified to pH = 6 and extracted with DCM (2 x 20 mL). The combined DCM extracts were dried over sodium sulfate and concentrated to give 4-((*tert*-butoxycarbonyl)(pyridin-4-yl)amino)butanoic acid (690 mg, 62% yield) as a dark green solid which was carried forward as is. LCMS t_r = 0.56 min, *m/z* [M+H$^+$] 281.3. **30a** prepared by the general procedure for NAP formation using 4-((*tert*-butoxycarbonyl)(pyridin-4-yl)amino)butanoic acid (690 mg, 2.46 mmol, 1 equiv), *N*-hydroxyphthalimide (402 mg, 2.46 mmol, 1 equiv), DMAP (15 mg, 0.12 mmol, 0.05 equiv), DIC (0.58 mL, 3.69 mmol, 1.5 equiv), and DCM (10 mL) with reagents mixed at 0 °C then warmed to room temp with reaction stirring for 22 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 4-((*tert*-butoxycarbonyl)(pyridin-4-yl)amino)butanoate (**30a**, 350 mg, 33% yield) as a yellowish solid. LC t_r = 0.92 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 8.53 - 8.45 (m, 2H), 7.88 - 7.82 (m, 2H), 7.79 - 7.73 (m, 2H), 7.27 - 7.22 (m, 2H), 3.87 - 3.81 (m, 2H), 2.69 (t, *J*=7.2 Hz, 2H), 2.06 (app quin, *J*=7.3 Hz, 2H), 1.47 (s, 9H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 169.0, 161.9, 153.3, 150.4, 149.5, 134.9, 128.9, 124.1, 118.9, 82.1, 47.6, 28.4, 28.3, 23.6; HRMS (ESI) *m/z* calcd for $C_{22}H_{24}N_3O_6$ [M+H$^+$] 426.1660, found 426.1651.



30b

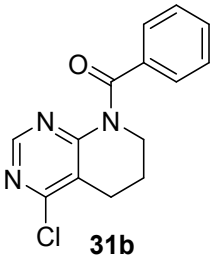
***tert*-butyl 3,4-dihydro-1,6-naphthyridine-1(2*H*)-carboxylate (30b).** Cyclization product prepared by the general procedure for intramolecular arene alkylation using **30a** (213 mg, 0.5 mmol, 1 equiv), 4CzIPN (**PC1**, 2 mg, 2.5 µmol, 0.5 mol %), and TFA (0.38 mL, 5.0 mmol, 10 equiv) in DMSO (25 mL) irradiating with purple light for 7 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave *tert*-butyl 3,4-dihydro-1,6-naphthyridine-1(2*H*)-carboxylate (**30b**, 77 mg, 66% yield) as a clear yellow liquid. LCMS t_r = 0.64 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 8.24 (d, *J*=5.9 Hz, 1H), 8.22 (s, 1H), 7.81 (d, *J*=5.9 Hz, 1H), 3.77 - 3.67 (m, 2H), 2.71 (t, *J*=6.3 Hz, 2H), 1.96 - 1.87 (m, 2H), 1.52 (s, 9H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 153.3, 150.0, 147.7, 145.6, 123.5, 116.3, 82.1, 45.4, 28.4, 25.1, 22.4; HRMS (ESI) *m/z* calcd for $C_{13}H_{19}N_2O_2$ [M+H$^+$] 235.1441, found 235.1435.



31a

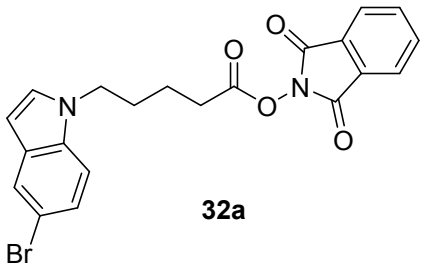
1,3-dioxoisoindolin-2-yl 4-(*N*-(6-chloropyrimidin-4-yl)benzamido)butanoate (31a). *tert*-butyl 4-aminobutanoate hydrochloride (1 g, 5.11 mmol, 1.0 equiv) and 4,6-dichloropyrimidine (0.837 g, 5.62 mmol, 1.1 equiv) were dissolved in anhydrous DMF (3 mL). Et_3N (1.78 mL, 12.8 mmol, 2.5 equiv) was added dropwise at 0 °C under a nitrogen atmosphere. The mixture was stirred at room temperature for 2 h. Upon completion, saturated aqueous sodium bicarbonate solution (20 mL) and water (5 mL) were added. The mixture was extracted with ethyl acetate (10 mL; 2x5 mL). The combined organic layer was dried over sodium sulfate, filtered, and concentrated. Flash column chromatography using silica gel on a Teledyne Isco instrument gave *tert*-butyl 4-((6-chloropyrimidin-4-yl)amino)butanoate (1.3 g, 94% yield) as a white solid. LCMS t_r = 0.84 min, *m/z* [M+H$^+$] 272.5. To a stirred solution of *tert*-butyl 4-((6-chloropyrimidin-4-yl)amino)butanoate (890 mg, 3.28 mmol, 1.0 equiv) and Et_3N (1.37 mL, 9.83 mmol, 3.0 equiv) in anhydrous 1,2-dichloroethane (5 mL) was added benzoyl chloride (0.57 mL, 4.91 mmol, 1.5 equiv) dropwise. The solution was stirred at room temperature for 19 h. Upon completion, the reaction was quenched by the addition of saturated aqueous sodium bicarbonate solution (10 mL). The aqueous layer was separated and extracted with ethyl acetate (3 x 3 mL). The combined organic layer was dried over sodium sulfate, filtered, and concentrated. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave *tert*-butyl 4-

(*N*-(6-chloropyrimidin-4-yl)benzamido)butanoate (1.20 g, 97% yield) as a clear yellow oil. LCMS t_r = 1.02 min, *m/z* [M+H$^+$] 376.3. To a stirred solution of *tert*-butyl 4-(*N*-(6-chloropyrimidin-4-yl)benzamido)butanoate (1.0 g, 2.66 mmol) in DCM (10 mL) was added TFA (5 mL) at 0 °C. The mixture was stirred at room temperature for 1.5 h. Upon completion, toluene (15 mL) was added and the mixture was concentrated. The residue was dissolved in DCM (5 mL) and toluene (15 mL) was added. The mixture was concentrated again to give crude 4-(*N*-(6-chloropyrimidin-4-yl)benzamido)butanoic acid which was assumed quantitative and carried forward as is into NAP formation. This material was dissolved in anhydrous DCM (25 ml). *N*-hydroxyphthalimide (1.30 g, 7.98 mmol, 3 equiv), and DMAP (16 mg, 0.13 mmol, 0.05 equiv) were added. DIC (1.67 mL, 10.6 mmol, 4 equiv) was then added dropwise at 0 °C under a nitrogen atmosphere. The reaction was stirred for 20 h at room temperature. The crude material was filtered, concentrated, and purified by flash column chromatography using silica gel on a Teledyne Isco instrument to give 1,3-dioxoisoindolin-2-yl 4-(*N*-(6-chloropyrimidin-4-yl)benzamido)butanoate (**31a**, 1.2 g, 97% yield) as a white solid. LCMS t_r = 0.93 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 8.81 (s, 1H), 7.94 - 7.85 (m, 2H), 7.84 - 7.73 (m, 2H), 7.52 - 7.43 (m, 3H), 7.43 - 7.34 (m, 2H), 6.86 (s, 1H), 4.28 (br t, *J*=7.0 Hz, 2H), 2.82 (t, *J*=7.2 Hz, 2H), 2.19 (quin, *J*=7.1 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 171.9, 169.1, 163.1, 162.0, 160.8, 158.6, 134.9, 134.8, 132.0, 129.0, 128.5, 124.1, 115.4, 46.9, 28.7, 23.5; HRMS (ESI) *m/z* calcd for $C_{23}H_{18}N_4O_5Cl$ [M+H$^+$] 465.0960, found 465.0961.



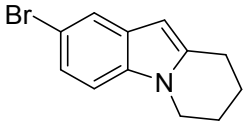
31b

(4-chloro-6,7-dihydropyrido[2,3-d]pyrimidin-8(5*H*)-yl)(phenyl)methanone (31b). Cyclization product prepared by the general procedure for intramolecular arene alkylation using **31a** (232 mg, 0.5 mmol, 1 equiv), 4CzIPN (**PC1**, 2 mg, 2.5 µmol, 0.5 mol %), and TFA (0.38 mL, 5.0 mmol, 10 equiv) in DMSO (25 mL) irradiating with purple light for 12 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave (4-chloro-6,7-dihydropyrido[2,3-d]pyrimidin-8(5*H*)-yl)(phenyl)methanone (**31b**, 82 mg, 60% yield) as a yellowish solid. LCMS t_r = 0.86 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 8.10 (s, 1H), 7.50 - 7.40 (m, 3H), 7.36 - 7.29 (m, 2H), 4.01 - 3.93 (m, 2H), 2.92 (t, *J*=6.8 Hz, 2H), 2.23 - 2.14 (m, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 172.0, 160.3, 159.7, 154.5, 136.5, 131.3, 128.4, 128.3, 117.2, 44.2, 24.2, 22.1; HRMS (ESI) *m/z* calcd for $C_{14}H_{13}N_3OCl$ [M+H$^+$] 274.0742, found 274.0745.



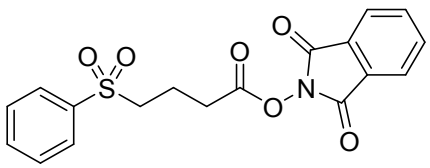
32a

1,3-dioxoisoindolin-2-yl 5-(5-bromo-1*H*-indol-1-yl)pentanoate (32a). NAP prepared by the general procedure for NAP formation using 5-(5-bromo-1*H*-indol-1-yl)pentanoic acid (450 mg, 1.52 mmol, 1 equiv), *N*-hydroxyphthalimide (273 mg, 1.67 mmol, 1.1 equiv), DMAP (9 mg, 0.08 mmol, 0.05 equiv), DIC (0.36 mL, 2.28 mmol, 1.5 equiv), and DCM (5 mL) with reagents mixed at 0 °C then warmed to room temp with reaction stirring for 3 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 5-(5-bromo-1H-indol-1-yl)pentanoate (**32a**, 660 mg, 98% yield) as yellowish solid. LC t_r = 1.39 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.89 - 7.83 (m, 2H), 7.80 - 7.74 (m, 2H), 7.73 (d, *J*=1.7 Hz, 1H), 7.28 (dd, *J*=8.8, 1.9 Hz, 1H), 7.21 (d, *J*=8.8 Hz, 1H), 7.11 (d, *J*=3.1 Hz, 1H), 6.43 (dd, *J*=3.1, 0.4 Hz, 1H), 4.13 (t, *J*=6.9 Hz, 2H), 2.65 (t, *J*=7.1 Hz, 2H), 2.03 - 1.93 (m, 2H), 1.82 - 1.71 (m, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 169.2, 162.0, 134.9, 134.7, 130.4, 128.9, 128.9, 124.4, 124.0, 123.5, 112.7, 110.8, 101.0, 46.0, 30.6, 29.2, 22.2; HRMS (ESI) *m/z* calcd for $C_{21}H_{18}N_2O_4Br$ [M+H$^+$] 441.0444, found 441.0451 and 443.0431 [(M+2)+H$^+$].



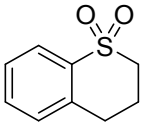
32b

2-bromo-6,7,8,9-tetrahydropyrido[1,2-a]indole (32b). Cyclization product prepared by the general procedure for intramolecular arene alkylation using **32a** (221 mg, 0.5 mmol, 1 equiv), 4CzIPN (**PC1**, 2 mg, 2.5 µmol, 0.5 mol %), and TFA (0.43 mL, 5.6 mmol, 11.2 equiv) in DMSO (25 mL) irradiating with purple light for 24 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 2-bromo-6,7,8,9-tetrahydropyrido[1,2-a]indole (**32b**, 35 mg, 28% yield) as a white solid containing a small amount of co-eluting impurities. LCMS t_r = 1.14 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.64 (d, *J*=1.9 Hz, 1H), 7.20 (dd, *J*=8.6, 1.9 Hz, 1H), 7.11 (d, *J*=8.6 Hz, 1H), 6.13 (app d, *J*=0.8 Hz, 1H), 4.01 (t, *J*=6.2 Hz, 2H), 2.97 (t, *J*=6.3 Hz, 2H), 2.13 - 2.04 (m, 2H), 1.93 - 1.85 (m, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 138.6, 135.1, 130.0, 122.9, 122.1, 113.0, 110.0, 97.3, 42.5, 24.3, 23.4, 21.1; HRMS (ESI) *m/z* calcd for $C_{12}H_{13}NBr$ [M+H$^+$] 250.0226, found 250.0231 and 252.0204 [(M+2)+H$^+$].



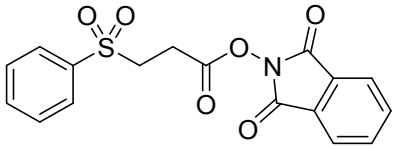
33a

1,3-dioxoisoindolin-2-yl 4-(phenylsulfonyl)butanoate (33a). NAP prepared by the general procedure for NAP formation using 4-(phenylsulfonyl)butanoic acid (685 mg, 3.0 mmol, 1 equiv), *N*-hydroxyphthalimide (809 mg, 4.96 mmol, 1.65 equiv), DMAP (17 mg, 0.14 mmol, 0.05 equiv), DIC (0.70 mL, 4.5 mmol, 1.5 equiv), and THF (15 mL) stirring for 19 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 4-(phenylsulfonyl)butanoate (**33a**, 1.04 g, 93% yield) as a clear oil that solidified into a white solid on standing. LCMS t_r = 0.86 min; ^{1}H NMR (499 MHz, CHLOROFORM-d) δ 7.98 - 7.93 (m, 2H), 7.91 - 7.86 (m, 2H), 7.82 - 7.77 (m, 2H), 7.70 - 7.65 (m, 1H), 7.62 - 7.57 (m, 2H), 3.32 - 3.26 (m, 2H), 2.86 (t, *J*=7.1 Hz, 2H), 2.26 - 2.18 (m, 2H); ^{13}C{^{1}H} NMR (126 MHz, CHLOROFORM-d) δ 168.5, 161.9, 138.9, 135.0, 134.1, 129.6, 129.0, 128.2, 124.2, 54.7, 29.5, 18.3; HRMS (ESI) *m/z* calcd for $C_{18}H_{16}NO_6S$ [M+H$^+$] 374.0693, found 374.0686.



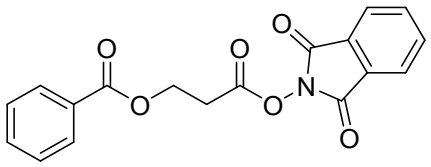
33b

thiochromane 1,1-dioxide (33b). Cyclization product prepared by the general procedure for intramolecular arene alkylation using **33a** (187 mg, 0.5 mmol, 1 equiv), 4CzIPN (**PC1**, 2 mg, 2.5 µmol, 0.5 mol %), and TFA (0.38 mL, 5.0 mmol, 10 equiv) in DMSO (25 mL) irradiating with purple light for 25 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave thiochromane 1,1-dioxide (**33b**, 28 mg, 31% yield) as a light yellow solid. LCMS t_r = 0.65 min; ^{1}H NMR (499 MHz, CHLOROFORM-d) δ 7.91 (dd, *J*=7.8, 1.0 Hz, 1H), 7.45 (td, *J*=7.5, 1.3 Hz, 1H), 7.40 (app t, *J*=7.7 Hz, 1H), 7.23 (d, *J*=7.7 Hz, 1H), 3.38 - 3.32 (m, 2H), 3.02 (t, *J*=6.4 Hz, 2H), 2.53 - 2.46 (m, 2H); ^{13}C{^{1}H} NMR (126 MHz, CHLOROFORM-d) δ 139.1, 136.5, 132.4, 129.7, 127.8, 123.8, 50.9, 28.5, 21.1; HRMS (ESI) *m/z* calcd for $C_9H_{11}O_2S$ [M+H$^+$] 183.0474, found 183.0473.



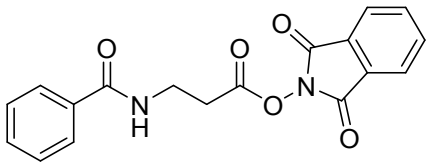
34a

1,3-dioxoisoindolin-2-yl 3-(phenylsulfonyl)propanoate (34a). NAP prepared by the general procedure for NAP formation using 3-(phenylsulfonyl)propanoic acid (536 mg, 2.5 mmol, 1 equiv), *N*-hydroxyphthalimide (673 mg, 4.13 mmol, 1.65 equiv), DMAP (15 mg, 0.13 mmol, 0.05 equiv), DIC (0.58 mL, 3.75 mmol, 1.5 equiv), and THF (12.5 mL) stirring for 6.5 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 3-(phenylsulfonyl)propanoate (**34a**, 750 mg, 83% yield) as a white solid. LCMS t_r = 0.85 min; ^{1}H NMR (499 MHz, CHLOROFORM-d) δ 7.99 - 7.94 (m, 2H), 7.91 - 7.85 (m, 2H), 7.82 - 7.77 (m, 2H), 7.74 - 7.69 (m, 1H), 7.65 - 7.60 (m, 2H), 3.56 - 3.50 (m, 2H), 3.19 - 3.12 (m, 2H); ^{13}C{^{1}H} NMR (126 MHz, CHLOROFORM-d) δ 166.9, 161.6, 138.3, 135.1, 134.5, 129.8, 128.9, 128.4, 124.3, 50.9, 25.4; HRMS (ESI) *m/z* calcd for $C_{17}H_{14}NO_6S$ [M+H$^+$] 360.0536, found 360.0534.



35a

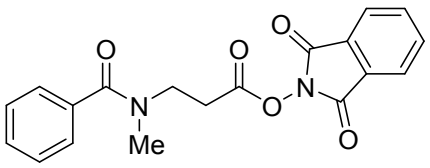
3-((1,3-dioxoisoindolin-2-yl)oxy)-3-oxopropyl benzoate (35a). To a stirred solution of benzyl 3-hydroxypropionate (1 g, 5.55 mmol, 1.0 equiv) and Et_3N (0.77 mL, 5.55 mmol, 1.0 equiv) in anhydrous DCM (10 mL) was added benzoyl chloride (0.78 mL, 6.66 mmol, 1.2 equiv) at -78 °C under a nitrogen atmosphere. The temperature was slowly raised to room temperature, and the mixture was stirred for 2 h at room temperature. Saturated aqueous sodium bicarbonate solution (15 mL) was added. The mixture was extracted with DCM (2 x 10 mL). The combined organic extracts were dried over sodium sulfate, filtered, and concentrated. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 3-(benzyloxy)-3-oxopropyl benzoate (1.17 g, 74% yield) as a clear liquid. LCMS (with 0.01 M NH_4OAc buffer) t_r = 1.01 min, *m/z* [M+H$^+$] 285.1. A mixture of 3-(benzyloxy)-3-oxopropyl benzoate (1.17 g, 4.12 mmol, 1.0 equiv), 10% Pd-C (0.11 g, 0.103 mmol, 0.025 equiv), and EtOAc (15 mL) was stirred under a hydrogen balloon for 4 h at room temperature. The mixture was filtered. The filtrate was concentrated to give 3-(benzoyloxy)propanoic acid (770 mg, 96% yield) as a white solid. LCMS (with 0.01 M NH_4OAc buffer) t_r = 0.41 min, *m/z* [M+H$^+$] 195.1. **35a** prepared by the general procedure for NAP formation using 3-(benzoyloxy)propanoic acid (485 mg, 2.50 mmol, 1 equiv), *N*-hydroxyphthalimide (448 mg, 2.75 mmol, 1.1 equiv), DMAP (15 mg, 0.13 mmol, 0.05 equiv), DIC (0.58 mL, 3.75 mmol, 1.5 equiv), and DCM (10 mL) with reagents mixed at 0 °C then warmed to room temp with reaction stirring for 16 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 3-((1,3-dioxoisoindolin-2-yl)oxy)-3-oxopropyl benzoate (**35a**, 137 mg, 16% yield). LCMS (with 0.01 M NH_4OAc buffer) t_r = 0.94 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 8.11 - 8.05 (m, 2H), 7.89 - 7.82 (m, 2H), 7.79 - 7.73 (m, 2H), 7.58 - 7.52 (m, 1H), 7.48 - 7.40 (m, 2H), 4.70 (t, *J*=6.1 Hz, 2H), 3.16 (t, *J*=6.2 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 167.1, 166.2, 161.7, 134.9, 133.3, 129.9, 129.6, 128.9, 128.5, 124.1, 59.4, 31.2; HRMS (ESI) *m/z* calcd for $C_{18}H_{14}NO_6$ [M+H$^+$] 340.0816, found 340.0819.



36a

1,3-dioxoisoindolin-2-yl 3-benzamidopropanoate (36a). NAP prepared by the general procedure for NAP formation using 3-benzamidopropanoic acid (386 mg, 2.0 mmol, 1.0 equiv), *N*-hydroxyphthalimide (538 mg, 3.30 mmol, 1.65 equiv), DMAP (12 mg, 0.10 mmol, 0.05 equiv), DIC (0.47 mL, 3.0 mmol, 1.5 equiv), and THF (10 mL) stirring for 18 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 3-benzamidopropanoate (**36a**, 615 mg, 91% yield) as a white

solid. LCMS t_r = 0.81 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.95 - 7.88 (m, 2H), 7.87 - 7.78 (m, 4H), 7.54 - 7.48 (m, 1H), 7.47 - 7.38 (m, 2H), 7.02 - 6.88 (m, 1H), 3.93 (q, *J*=6.1 Hz, 2H), 3.02 (t, *J*=5.9 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-d) δ 168.9, 167.8, 162.1, 135.1, 134.1, 131.8, 129.0, 128.7, 127.3, 124.3, 35.8, 32.3; HRMS (ESI) *m/z* calcd for $C_{18}H_{15}N_2O_5$ [M+H$^+$] 339.0975, found 339.0977.



37a

1,3-dioxoisoindolin-2-yl 3-(*N*-methylbenzamido)propanoate (37a). 3-(methylamino)propanoic acid, HCl (400 mg, 2.87 mmol, 1.0 equiv) was stirred in water (9.6 mL) until dissolved. THF (19.1 mL) was added. Aqueous sodium hydroxide (1 M, 2.87 mL, 2.87 mmol, 1.0 equiv) was then added slowly, and the reaction was stirred at room temperature for 5 minutes. Benzoyl chloride (0.33 mL, 2.87 mmol, 1.0 equiv) was added dropwise and then the reaction was stirred at room temperature for 80 minutes. Then, another aliquot of benzoyl chloride (0.33 mL, 2.87 mmol, 1.0 equiv) was added to the reaction mixture and the reaction was stirred at room temperature for 80 minutes more. Upon completion, the reaction was quenched by the addition of 1M aqueous HCl until pH < 4, as judged by pH paper. The reaction was then diluted with DCM (25 mL) and water (25 mL). The reaction was extracted 2x with 15-20 mL of DCM. The combined organic layer was dried over sodium sulfate, filtered, and concentrated. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 3-(*N*-methylbenzamido)propanoic acid (208 mg, 35% yield). LCMS t_r = 0.55 min, *m/z* [M+H$^+$] 208.0. **37a** prepared by the general procedure for NAP formation using 3-(*N*-methylbenzamido)propanoic acid (208 mg, 1.0 mmol, 1.0 equiv), *N*-hydroxyphthalimide (270 mg, 1.66 mmol, 1.65 equiv), DMAP (6 mg, 0.05 mmol, 0.05 equiv), DIC (0.24 mL, 1.51 mmol, 1.5 equiv), and THF (5 mL) stirring for 15.5 h. Purification by flash column chromatography using silica gel on a Teledyne Isco instrument gave 1,3-dioxoisoindolin-2-yl 3-(*N*-methylbenzamido)propanoate (**37a**, 323 mg, 91% yield) as a white solid containing small amounts of co-eluting impurities. LCMS t_r = 0.84 min; ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.93 - 7.86 (m, 2H), 7.84 - 7.77 (m, 2H), 7.53 - 7.35 (m, 5H), 4.08 - 3.66 (m, 2H), 3.24 - 2.95 (m, 5H) (rotamers present); ^{13}C{^{1}H} NMR (126 MHz, CHLOROFORM-d) δ 172.0, 168.6 (br), 161.8 (br), 136.0, 134.9, 129.8, 128.9, 128.5 (br), 127.2 (br), 124.1, 44.3 (br), 39.2 (br), 29.7 (br) (rotamers present); HRMS (ESI) *m/z* calcd for $C_{19}H_{17}N_2O_5$ [M+H$^+$] 353.1132, found 353.1140.

ASSOCIATED CONTENT

Supporting Information

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

Full HTE results, mechanistic studies, and spectral data for all new compounds (PDF)

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Author Contributions

All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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(26) The yield for **17b** is partially depressed due to a co-eluting impurity which is carried through its synthesis.

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