Note

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Organo Photoinduced Decarboxylative Alkylation of Coumarins with N-(Acyloxy)phthalimide

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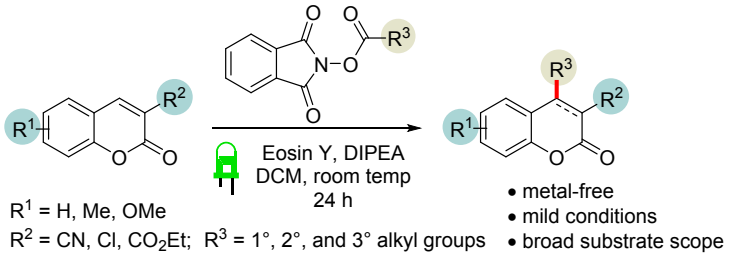


Abstract: A metal free and mild, photo-induced decarboxylative 4-position alkylation of coumarins has been reported. Photo-induced single electron transfer has been initiated by utilizing the visible-light absorptivity of Eosin Y for a reductive generation of alkyl radicals from N-(acyloxy)phthalimide esters. Depending on the nature of N-(acyloxy)phthalimide esters (primary, secondary, and tertiary carboxylic acid derived) several saturated and unsaturated C-4 alkylated coumarins were synthesized. Both control experiments and photophysical studies supported a radical based mechanism for the selective alkylation.

Visible light catalyzed selective construction of carbon-carbon bond has started to garner attention from chemists recently.[1] The attractiveness of such selective photoreactions are attributed to the synthetic utility of a photo active catalyst, which on excitation by appropriate wavelength functions as single electron or energy transfer source to yield free radical intermediates.[2] Many metals based homogeneous photo redox catalysts such as ruthenium and iridium complexes, and heterogeneous semiconductor catalyst have been

extensively explored for various synthetic transformations.[3] On the contrary, while many organic dyes have demonstrated photocatalytic activities, their use as catalyst for reactions that enables previously inaccessible synthetic transformations are scarce in selective organic synthesis.[4] For example, it has been reported that aliphatic carboxylic acids and their derivatives can generate a corresponding alkyl radical by photo-redox mediated single electron transfer and CO_2 extrusion mechanism. Typically, the alkyl radical can be generated either by esterification of the acid followed by reductive cleavage of the esters[5a-c] or by direct oxidative cleavage of the acid.[5d-f] Similar reactions that uses the low energy visible light has been utilized to achieve photocatalytic decarboxylative reactions such as arylations,[6a] fluorinations,[6b] vinylations,[6c] allylations[6d] and alkynylations.[6e] It has been demonstrated that *in situ* generated radicals can then react with the activated alkene to yield corresponding analogues[7]. Recently, Eosin Y has been extensively used as a catalyst to achieve various photochemical transformations.

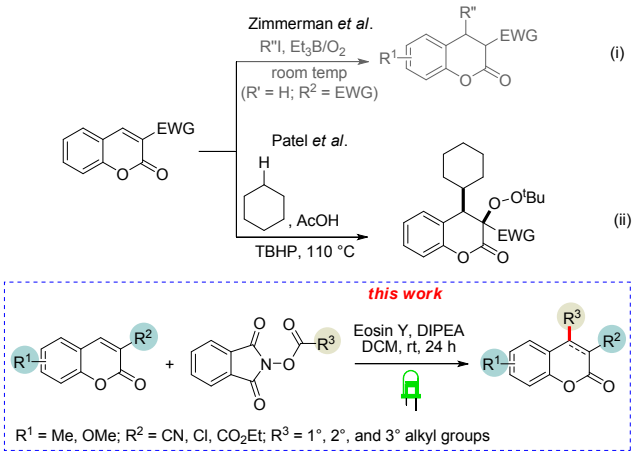
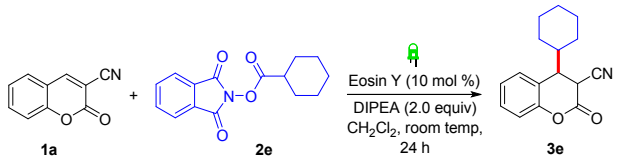


Fig. 1. Previous Contributions and Current Approach for Alkylation of Coumarins.

König and coworkers have demonstrated, Eosin Y catalyzed decarboxylative alkylation of acrylates from N-(acyloxy)phtalimide esters.[5a] Interestingly, while one can find many examples of alkylation of monosubstituted and disubstituted alkene, the trisubstituted alkene alkylations are limited. Addressing the

lacuna, in our present protocol, we have attempted to explore the reactivity of the radical intermediates generated by photocatalytic decarboxylation of N-(acyloxy)pthalimide esters with 3-substituted coumarins and its analogues. Coumarins are naturally occurring compounds and have utility in organic materials for optical property[8a-c] and in pharmaceuticals for anti-inflammatory, anti-oxidant, antimicrobial and anti-cancer bio-activities.[8d-g] Various approaches such as nucleophilic addition to Michael acceptor, direct C-H functionalization through oxidative cross coupling reaction with metal or without metal have been explored for the synthesis of coumarin derivatives.[9] However, the alkylation of coumarins yielding chain alkylated derivatives and other highly functionalized scaffold installation through alkylation *via* oxidative coupling reaction is still an arduous task. To the best of our knowledge, thus far there is no report on such alkylation of coumarin at C-4 position except Zimmerman's report,[10a] which could provide the alkylation of coumarins by a metal free approach (Fig. 1, eq. i). Recently, Patel[10b] demonstrated a similar alkylation method of coumarin using TBHP as an oxidant ended in di-functionalization (an alkylation at C-4 and peroxidation at C-3) (Fig. 1, eq. ii). In all the reports while it's commendable that the reactions were direct and without any side products the limited substrate scopes and high temperature reactions limits them for post synthesis functional group manipulations. While preparing our manuscript, Sun[11] reported visible–light induced Ir catalyzed regioselective, decarboxylative C-3 alkylation of coumarin, although with limited substrate scope. In the present work we are reporting a photocatalyzed approach to access a library of alkylated coumarins where several phthalimide esters have been used as source of alkyl radicals. Interestingly, we could isolate the saturated and unsaturated products depending on the nature of the phthalimide esters used.

Table 1.[a] Selected Optimization Reaction Condition Results.



1a **2e** **3e**

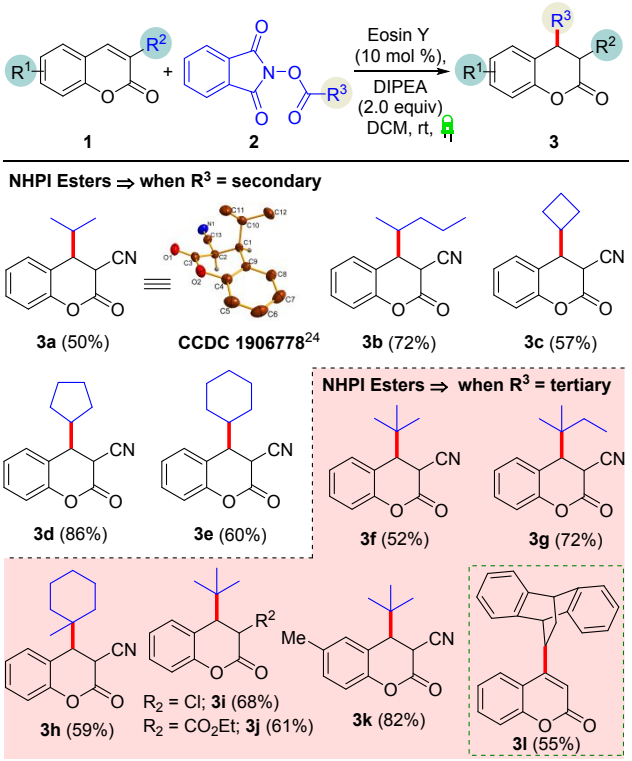
entry	deviation from above	yield (%)[b]
1	none	60
2	in the absence of Eosin Y	ND
3	in the absence of DIPEA	ND
4	in the absence of light	ND
5	5 mol % Eosin Y	42
6	5 mol % of $Ru(bpy)_2PF_6$ instead of Eosin Y	30
7	10 mol % of Mes-Acr$^+$ instead of Eosin Y	ND
8	10 mol % of Rose Bengal instead of Eosin Y	20
9	CH_3CN instead of CH_2Cl_2	35
10	DMF instead of CH_2Cl_2	ND
11	$CHCl_3$ instead of CH_2Cl_2	22
12	$C_2H_4Cl_2$ instead of CH_2Cl_2	45
13	Et_3N instead of DIPEA	ND

[a]Reaction Conditions **1a**:**2e** = 1.2:1, for 0.2 mmol scale, solvent 3mL. [b]Isolated yield. DIPEA = N,N-Diisopropylethylamine, ND = not detected, Mes-Acr$^+$ = 9-Mesityl-10-methylacridinium tetrafluoroborate.

Our study was initiated by an investigation of the proposed alkylation of 3-cyanocoumarins (**1**) and N-(acyloxy) phthalimide of cyclohexyl carboxylic acid (**2e**) as model substrates for the decarboxylative alkylation in the presence of photoredox catalyst under a green LED irradiation. After extensive screening we were delighted to established that a combination of Eosin Y (10 mol %), DIPEA (2.0 equiv.) in dichloromethane (0.08 M) under photo-irradiation at room temperature was optimum, affording the desired product **3e** in 60% isolated yield (Table 1, entry 1). Control experiments indicated that deviation from the optimal condition led to either no product or significant drop in the yield of **3e**. Notably, in the absence of any reaction component such as Eosin Y or DIPEA or visible-light irradiation, no alkylated product was observed (Table 1, entry 2-4). Lowering of catalyst loading from 10 mol % to 5 mol % yielded lower conversion (Table 1, entry 5). Eosin Y was the only effective photocatalyst and with other photocatalyst no improvement in yield of the product was observed. The common Ru metallic photocatalyst (Table 1, entry 6) or other organo-photocatalysts such as Mes-Acr$^+$ and Rose Bengal were

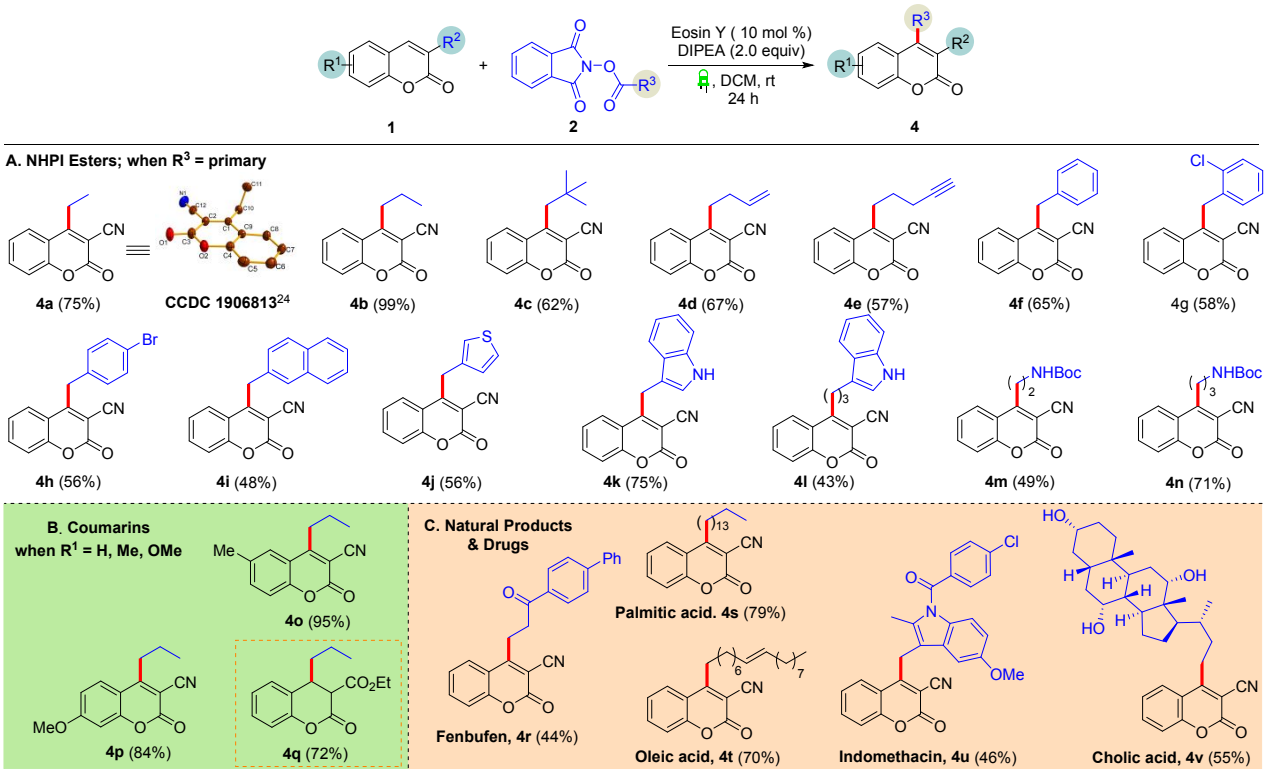
least effective (Table 1, entry 7, 8). The choices of solvents played critical role in optimizing the reaction outcome. Switching reaction solvent from DCM to acetonitrile or $CHCl_3$ or DMF or DCE produced alkylated product in much lower yield (Table 1, entry 9-12). A survey of organic bases revealed that the DIPEA was the best choice. Replacing DIPEA with Et_3N yielded no product (Table 1, entry 13). The substrate scope, which ensued from the above optimized reaction conditions is summarized in Table 2 and Table 3. Unexpectedly, secondary carboxylic acids derived NHPI esters when coupled with 3-substituted coumarins under optimized reaction conditions provided 3,4-substituted 2-chromanone instead of 3,4-substituted 2-chromenones. NHPI esters of isobutyric and 2,2-dimethylbutanoic acids provided 4-(2-propyl) and 4-(2-pentyl) substituted 3-cyano-2-chromanones **3a** and **3b** in 50% and 72% of isolated yields, respectively (Table 2). Structure of **3a** was unambiguously confirmed by single crystal XRD (CCDC no. 1906778). Secondary carboxylic acids appended to acyclic chains (cyclobutyl, cyclopentyl and cyclohexyl) were converted into corresponding 4-alkylated 2-chromanones products with 57%-86% of isolated yields (Table 2, entries **3c**-**3e**). In lieu of above results, we tried pivalic, 2,2-dimethylbutanoic and 1-methyl-1-cyclohexane tertiary aliphatic carboxylic acids derived NHPI esters. Coherently, we obtained 52%-82% of isolated yield of 4-alkylated products when pivalic acid derived NHPI ester has been used with various coumarins {Table 2, R^2 = CN (**3f**), Cl (**3i**) and CO_2Et (**3j**)}. NHPI esters of 2,2-dimethylbutanoic and 1-methyl-1-cyclohexane tertiary aliphatic carboxylic acids gave 72% and 59% of isolated yield of 4-alkylated 3-cyano-2-chromanones (Table 2, entry **3g**, **3h**). NHPI ester derived from 9,10-dihydro-9,10-ethanoanthracene-11-carboxylic acid gave anomalous result in which we observed unsaturation with elimination of nitrile group (Table 2, entry **3l**, yield 55%).

Table 2.[a] Scope of decarboxylative 4-position alkylation of coumarins with various secondary and tertiary carboxylic acid derived NHPI esters.



[a]Reaction conditions: All the reactions were carried out with 0.24 mmol of **1** and 0.2 mmol of **2** in the presence of 10 mol % of Eosin Y in 3 mL of DCM at room temperature under green light irradiation.

Table 3.[a] **Scope of decarboxylative 4-position alkylation of coumarins with various primary carboxylic acid derived NHPI esters.**

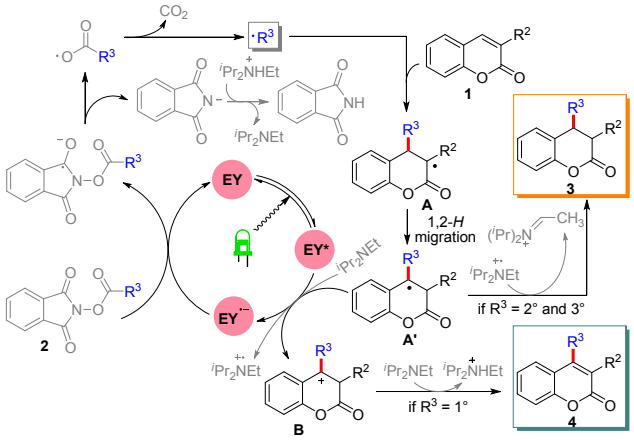


[a]Reaction conditions: All the reactions were carried out with 0.24 mmol of **1** and 0.2 mmol of **2** in presence of 10 mol% of Eosin Y in 3 mL of DCM at room temperature under green light irradiation.

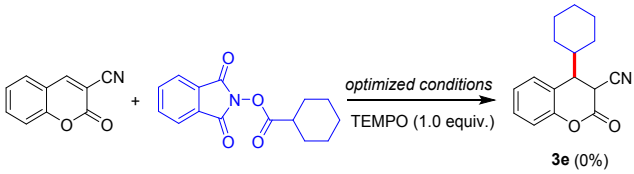
Primary carboxylic acid derived NHPI esters produced surprising results when used with 3-substituted coumarins under this visible-light mediated decarboxylative alkylation strategy (Table 3). In this process, primary carboxylic acids of alkyl, branched alkyl, β-positioned alkene, γ-positioned alkyne, benzylic substrates, substrates bearing extended aromatics, heterocycles (thiophene, indole) and amino acids (β-alanine and γ-alanine) were converted into the corresponding 4-alkylated-3-cyanocoumarins in good to high yields *via* their phthalimide esters (Table 3, Part A, entry **4a**-**4n**). Functional variations on coumarins itself with electron donating 6-Me and 7-OMe groups supported this alkylation well with yields up to 95%

(Table 3, Part B, entry **4o**, **4p**). In case when we made an attempt to alkylate ethyl 3-coumarincarboxylate, we observed saturated instead of unsaturated coumarin **4q** in 72% yield (Table 3, Part B).

Scheme 1. Plausible mechanism of alkylation.



Scheme 2. Control Experiment.



To showcase the utility of the transformation for diversifying natural-products and drugs caboxylic acids, we prepared a diverse collection of *N*-(aceloxy)phthalimide esters and subjected them to the optimized reaction conditions (Table 3, Part C, entry **4r-4v**, 44%-79% yield). The proposed mechanism illustrated in Scheme 1 can be rationalized by spectroscopic and electrochemical studies performed on control reactions (Supporting Information) and based on similar observations in the literature.[4b,5a] Photo-irradiation *via* the green LED, excites Eosin Y leading to single electron transfer (SET) from DIPEA (0.72 V vs SCE in CH_3CN) to excited Eosin Y* (Eosin Y*/Eosin $Y^{\bullet-}$ = 0.83 V vs SCE in CH_3CN-H_2O, 1:1) (Scheme 1). Following this, regeneration of Eosin Y take place by single electron reduction of NHPI ester (-1.20 V vs SCE in CH_3CN-H_2O, 1:1). The reduced ester produces $^{\bullet}R^3$ after breaking of the N–O bond

and subsequent elimination of CO_2. To confirm the formation of radical $^{\bullet}R^3$, we performed radical trapping experiment with 1.0 equiv. of TEMPO. Presence of radical trapper inhibited the reaction and no product formation was observed (Scheme 2), thus, confirming the radical pathway. The $^{\bullet}R^3$ is then added on coumarin and generates an open radical **A**. Further, intramolecular 1,2-hydrogen migration took place which facilitated the generation of 4-positioned benzylic radical **A'**. We hypothesized two possible pathways of terminations. First, if $^{\bullet}R^3$ is secondary or tertiary then oxidized DIPEA will transfer $H^{\bullet}$ to **A'** and consequently formation of **3** will be observed. Secondly, if $^{\bullet}R^3$ is primary then **A'** will get oxidized by Eosin Y* and **B** will be formed, which will produce **4** after abstraction of H^+ by DIPEA. Since Eosin Y has a fluorescence emission (λ_{em} = 550nm, λ_{ex} = 520nm) it can be used to study the structural changes in Eosin Y by observing the changes in the fluorescence emission. When the Fluorescence spectra of Eosin Y and NHPI were recorded no significant difference in the fluorescence peak (Supporting Information, Figure S1) was observed suggesting very poor quenching due to any electron transfer. Similarly addition of coumarin to Eosin Y and NHPI mixture did not alter the fluoresce emission (Supporting Information, Figure S1). However, when the same reaction was monitored with addition of DIPEA, a significant quenching of the fluorescence emission was observed over time with almost no emission after 8 h (Supporting Information, Figure S2), thus, suggesting an electron transfer with DIPEA.

In conclusion, we have developed a mild, metal-free, low energy (visible-light) mediated organo-photocatalyzed strategy for 4-alkylation of 3-substituted coumarins. Primary carboxylic acids derived NHPI esters produced 4-alkylated 3-substituted saturated coumarins while those of secondary and tertiary carboxylic acids produced 4-alkylated 3-substituted unsaturated coumarins. We believe that developed methodology offers a powerful post-synthetic modification route for generating various new classes of highly functionalized small molecules.

Experimental Section

General Information. The *N*-(acyloxy)phthalimide esters have been prepared from the commercially available corresponding carboxylic acids and *N*-hydroxyphthalimides. Nuclear magnetic resonance (NMR) spectra were recorded in deuterated solvents with residual protonated solvent signal as internal reference on a BrückerAva-300, BrückerAva-400 and BrückerAva-500. Chemical shifts are reported in parts per million using the solvent resonance internal standard (chloroform, 7.26 and 77.0 ppm or DMSO, 2.50 and 40.0 ppm). Data is reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, bs = broad singlet), coupling constant, and integration. Electrospray and electron impact high resolution mass spectrometry was performed by Brücker mass spectrometer. The data is recorded as the ionization method followed by the calculated and measured masses. Solvents for starting material preparation and coupling reactions were dried before use. Green LEDs (2.50 W, λ = 530 nm) Rebel LED, mounted on a 25 mm cool base was purchased from commercial supplier Luxeon Star LEDs Quadica Developments Inc.10-3447 30 Ave N. Lethbridge, Alberta T1H 7B5 Canada. No filter has been used. Glass material of round-bottom flask is of borosilicate. Distance of RB from LED was kept fixed at 5cm (see Supporting Information for photoreaction set-up).

General Method for the Synthesis of Starting Materials Coumarins (1) and N-(Acyloxy)phthalimide Esters (2)

2.1. Preparation of Coumarins

2.1.1. Preparation of 3-Cyanocoumarins (1a-c)

3-Cyanocoumarins were synthesized using known literature procedure.[12] To a solution of salicylaldehyde (10.0 mmol) and malononitrile (660 mg, 10.0 mmol) in EtOH (10.0 mL) was added NH_4OAc (462 mg, 6.0 mmol) slowly. The reaction mixture was stirred at room temperature for 4h to form the precipitations. Then the precipitate was filtered and washed with EtOH and dried in vacuum. Next, the products were dissolved in EtOH by gentle heating at 75 ^oC in oil bath and then 1 mL HCl was added in reaction mixture.

The resulting reaction mixture was vigorously stirred at 75 °C in oil bath for 30 min. Subsequently, it was poured in ice water. A solid precipitate was obtained. The resulting solid was filtered, washed with cold water and recrystallized in EtOH, yielded corresponding 3-cyanocoumarins.

2.1.2. Synthesis of ethyl coumarin-3-carboxylate (1d)

Ethyl coumarin-3-carboxylate **1d** were synthesized following known literature procedure.[13] To a solution of salicylaldehyde (1.83 g, 15 mmol) in 30 mL of ethanol was added diethyl malonate (2.88 g, 18 mmol), 2 drops of acetic acid and piperidine (0.15 mL). The reaction mixture was stirred under reflux for 8 h, and dilution was done with ice-cold water (50 mL). After completion of the reaction, the cake was filtered and washed with cold water. The product was dried under vacuum to give a white solid (3.07 g, 94% yield).

2.1.3. Synthesis of 3-Chlorocoumarin (1e)

3-Chlorocoumarin (**1e**) was synthesized following known literature procedure.[14] To a solution of coumarin (10 mmol) in 1M HCl-DMF (15 mL) solution was added *m*-CPBA (15 mmol). The reaction mixture was stirred at rt for 30 min. After completion, reaction was quenched with 1M $NaHCO_3$ and extracted with Et_2O (3 x 50 mL) after removal of solvent in vacuo, the product was purified by silica gel chromatography using EtOAc-hexane (1:4) as eluent.

2.2. Preparation of *N*-(acyloxy)phthalimides (2)

All N-(Acyloxy)phthalimides (**2a-2o, 2q-2t, 2w-2z,** and **2za**) were synthesized by following known literature procedures.[5a,15-23] The NHPI esters **2p**, **2u**, **2v**, and **2zb** were synthesized by following the known method of Koenig[5a] in which we took respective carboxylic acids (4.0 mmol, 1.0 equiv.), *N*-hydroxyphthalimide (721 mg, 4.40 mmol, 1.1 equiv.), *N*,*N*'-dicyclohexylcarbodiimide (988 mg, 4.8 mmol, 1.2 equiv.) and 4-dimethylaminopyridine (48 mg, 0.80 mmol, 0.1 equiv.) in a round bottom flask. Dry THF (20 mL) was added and the orange reaction mixture was stirred for 15 h at room temperature. After completion of reaction the white precipitate was filtered off and the solution was concentrated by

evaporation of the solvent. Purification by column chromatography on silica gel (EtOAc: hexane = 3:7) gave a solid **2**. All characterization data for **2p**, **2u**, **2v**, and **2zb** are reported.

3. General Methods of Preparations for the Synthesis of 3 and 4

0.2 mmol of *N*-(acyloxy)phthalimides (1.0 equiv.), coumarin (0.24 mmol, 1.2 equiv.) were taken in a long neck round bottom flask and 10 mol % of Eosin Y was added into it, the RB was capped with septum. After that 2.0 equiv. of DIPEA and then 3 ml of dry DCM were added into the reaction mixture via syringe. The mixture was degassed and filled with N_2 (three times). The reaction mixture was irradiated with green LED for 24 h. After completion (monitored through TLC), reaction was quenched with saturated $NaHCO_3$ solution and extracted with DCM (3 x 10 mL), washed with brine solution. After removal of solvent in vacuo, the product was purified by silica gel chromatography using EtOAc-hexane (1:9 to 4:6) as eluent to provide the desired product.

1,3-Dioxoisoindolin-2-yl 2-(2-chlorophenyl)acetate **(2p). Physical state**: White solid; **Yield**: 856.8 mg (68%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.89 – 7.87 (m, 2H), 7.80 – 7.77 (dd, *J* = 5.4, 2.8 Hz, 2H), 7.42 (s, 2H), 7.30 – 7.25 (m, 2H), 4.15 (d, *J* = 2.6 Hz, 2H). **^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$)** δ 166.9, 161.8, 134.9, 129.8, 129.5, 129.0, 127.3, 124.1, 35.8. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{16}H_{10}ClNO_4Na$, 338.0190; Found: 338.0180.

1,3-Dioxoisoindolin-2-yl 4-(1H-indol-3-yl)butanoate **(2t). Physical state**: yellow solid; **Yield:** 1.08 g, **(**78%**). ^{1}H NMR (300 MHz, $CDCl_3$)** δ 8.05 (s, 1H), 7.90 – 7.87 (m, 2H), 7.79 – 7.77 (m, 2H), 7.63 (d, *J* = 7.7 Hz, 1H), 7.37 (d, *J* = 7.9 Hz, 1H), 7.26 – 7.07 (m, 3H), 2.94 (t, *J* = 7.2 Hz, 2H), 2.70 (t, *J* = 7.1 Hz, 2H), 2.31 – 2.04 (m, 2H). **^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$)** δ 169.8, 162.1, 136.5, 134.8, 129.0, 127.4, 124.0, 122.1, 119.4, 114.7, 111.3, 30.3, 25.1, 24.0. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{20}H_{16}N_2O_4Na$, 371.1002; Found: 371.0990.

1,3-Dioxoisoindolin-2-yl 3-(tert-butoxycarbonylamino)propanoate **(2v). Physical state**: white solid; **Yield:** 1.01 g (76%)**. ^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.90- 7.71 (m, 4H), 5.15 (s, 1H), 3.55 (d, *J* = 5.8 Hz, 2H), 2.90 (t, *J* = 5.9 Hz, 2H), 1.44 (s, 9H). **^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$)** δ 168.6, 161.8, 155.8, 134.9, 128.8, 124.0, 79.8, 36.1, 32.1, 28.3. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{16}H_{18}N_2O_6Na$, 357.1057; Found: 357.1045.

2-Oxo-4-((3S)-3-((3S,5R,7S,8S,10R,12R,13S,14R,17S)-3,7,12-trihydroxy-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthren-17-yl)butyl)-2H-chromene-3-carbonitrile **(2zb). Physical state**: white solid; **Yield:** 1.15 g **(**52%)**. ^{1}H NMR (300 MHz, $CDCl_3$)** 7.88 (s, 2H), 7.79 (s, 2H), 4.00 (s, 1H), 3.85 (s, 1H), 3.45 (s, 1H), 2.64 (t, *J* = 16.4 Hz, 2H), 2.26 – 2.22 (m, 3H), 1.92 - 1.81 (m, 7H), 1.81 – 1.67 (m, 6H), 1.56 (s, 6H), 1.42 -1.31 (m, 3H), 1.24 (d, *J* = 7.1 Hz, 1H), 1.13 (d, *J* = 13.3 Hz, 2H), 0.89 (s, 3H), 0.72 (s, 3H). **^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$)** δ 170.2, 162.0, 134.7, 128.9, 123.9, 73.1, 71.9, 68.4, 60.4, 46.8, 41.5, 39.5, 35.4,35.1, 34.8, 30.7, 28.1, 27.5, 26.3, 22.3, 22.4, 21.0, 17.3, 14.2, 12.5. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{32}H_{43}NO_7Na$, 576.2931; Found: 576.2916.

4-Isopropyl-2-oxochromane-3-carbonitrile (**3a**). **Physical state**: White solid; **Yield**: 21.50 mg (50%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.36 – 7.32 (dd, *J* = 10.4, 4.2 Hz, 1H), 7.23 – 7.11 (m, 3H), 4.08 (d, *J* = 6.3 Hz, 1H), 3.30 (dd, *J* = 6.1, 4.0 Hz, 1H), 2.49-2.39 (m, 1H), 1.09 (d, *J* = 6.9 Hz, 3H), 0.80(d, *J* = 6.8 Hz, 3H). **^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$)** δ 161.9, 151.1, 129.8, 129.8, 125.0, 120.2, 117.5, 114.0, 44.6, 38.1, 30.6, 21.5, 16.8. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{13}H_{13}NO_2Na$, 238.0838; Found: 238.0832.

2-Oxo-4-(pentan-2-yl)chromane-3-carbonitrile (**3b**). **Physical state**: White solid; **Yield**: 35 mg (72%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.41 – 7.32 (m, 1H), 7.25 – 7.15 (m, 2H), 7.15 – 7.09 (m, 1H), 4.06 (t, *J* = 5.2 Hz, 1H), 4.01 (s, 1H), 3.41 (dd, *J* = 6.4, 3.2 Hz, 1H), 3.36 – 3.31 (m, 0.21H), 3.13 (d, *J* = 7.4 Hz,

0.50H), 2.27 (s, 1H), 1.67 (s, 3H), 1.49 – 1.35 (m, 6H), 1.21 (m, 4H), 1.08 (d, *J*= 6.9 Hz, 1H), 0.99 – 0.92 (m, 3H), 0.87 (m, 5H), 0.76 (d, *J* = 6.8 Hz, 3H). **$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$)** δ 161.9, 151.2, 150.7, 129.6, 125.1, 120.3, 117.5, 111.3, 46.3, 43.2, 38.2, 37.4, 35.4, 20.4, 14.1, 14.0. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{15}H_{17}NO_2Na$, 266.1151; Found: 266.1148.

4-Cyclobutyl-2-oxochromane-3-carbonitrile (**3c**)**. Physical state**: Brown gum; **Yield**: 25.88 mg (57%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.39 – 7.33 (m, 1H), 7.24-7.19 (m, 2H), 7.16-7.10 (m, 1H), 3.98 (d, *J* = 5.2 Hz, 1H), , 3.27 (dd, *J* = 7.9, 5.2 Hz, 1H), , 2.79-2.74 (m, 1H), 2.26 - 2.17 (m, 1H), 1.99-1.82 (m, 3H), 1.71 (bs, 1H), 0.98 – 0.80 (m, 1H). **$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$)** δ 161.1, 150.5, 129.7, 128.8, 125.3, 122.2, 117.5, 113.9, 43.8, 37.5, 37.4, 27.3, 26.1, 18.7. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{14}H_{13}NO_2Na$, 250.0839; Found: 250.0843.

4-Cyclopentyl-2-oxochromane-3-carbonitrile (**3d**). **Physical state**: Brown gum; **Yield**: 41.45 mg (86%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.39 – 7.36 (m, 1H), 7.29 – 7.21 (m, 2H), 7.18 - 7.13(m, 1H), 4.09 (d, *J* = 5.5 Hz, 1H), 3.43 (t, *J* = 5.7, Hz, 1H), 2.32-2.30 (m, 1H), 2.06-2.04 (m, 1H), 1.86 – 1.75 (m, 1H), 1.60 – 1.51 (m, 4H), 1.45 – 1.33 (m, 1H), 1.01 – 0.83 (m, 1H). **$^{13}C\{^{1}H\}$ NMR (CDCl3**, **101 MHz)** δ 161.7, 159.8, 1508, 129.7, 129.4, 125.5, 117.5, 114.2, 42.1, 42.5, 39.0, 31.1, 29.4, 24.3. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{15}H_{15}NO_2Na$, 264.0995; Found: 264.0997.

4-Cyclohexyl-2-oxochromane-3-carbonitrile (**3e**). **Physical state**: White solid; **Yield**: 35.70 mg (70%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.38 – 7.32 (m, 1H), 7.22 – 7.09 (m, 3H), 4.04 (dd, *J* = 4.4, 3.7 Hz, 1H), 3.26 (dd, *J* = 6.0, 3.7 Hz, 1H), 2.08 – 1.99 (m, 1H), 1.78 (t, *J* = 13.4 Hz, 2H), 1.63 (s, 2H), 1.39 – 1.07 (m, 4H), 1.04 – 0.82 (m, 1H), 0.79 – 0.65 (m, 1H). **$^{13}C\{^{1}H\}$ NMR (CDCl3**, **75 MHz)** δ 162.0, 151.0, 129.8, 129.7, 125.0, 121.7, 117.4, 114.0, 44.6, 40.4, 37.8, 31.5, 27.2, 26.2, 25.8, 25.7. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd For $C_{16}H_{17}NO_2Na$, 278.1151; Found: 278.1160.

4-(tert-Butyl)-2-oxochromane-3-carbonitrile (**3f**). **Physical state**: White solid; **Yield**: 23.82 mg (52%)**. ^{1}H NMR (300 MHz**, **$CDCl_3$)** δ 7.43 – 7.33 (m, 1H), 7.26-7.23 (m, 2H), 7.25- 7.16 (m, 1H), 4.12 (s, 1H), 3.05 (s, 1H), 0.98 (s, 9H). **^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$)** δ 160.6, 151.8, 131.4, 130.4, 125.9, 119.7, 117.7, 114.2, 51.8, 35.6, 33.4, 27.8. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd For $C_{14}H_{15}NO_2Na$, 252.0995; Found: 252.1004.

2-Oxo-4-(tert-pentyl)chromane-3-carbonitrile (**3g**). **Physical state**: White solid; **Yield**: 34.99 mg (72%)**. ^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.42 – 7.37 (m, 1H), 7.25 (d, *J* = 5.4 Hz, 2H), 7.22 – 7.15 (m, 1H), 4.09 (s, 1H), 3.15 (s, 1H), 1.37 (dd, *J* = 15.0, 7.5 Hz, 2H), 0.94-0.87 (m, 9H). **^{13}C{^{1}H} NMR ($CDCl_3$, 300 MHz)** δ 160.7, 151.2, 131.4, 129.9, 125.1, 119.7, 117.6, 114.7, 49.6, 37.7, 33.5, 31.9, 24.2, 23.3, 8.2. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{15}H_{17}NO_2Na$, 266.1151; Found: 266.1148.

4-(1-Methylcyclohexyl)-2-oxochromane-3-carbonitrile (**3h**). **Physical state**: White solid; **Yield**: 34.45 mg (59%). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.41 – 7.38 (m, 1H), 7.26 – 7.20 (m, 2H), 7.16 (d, *J* = 8.2 Hz, 1H), 4.16 (s, 1H), 3.12 (s, 1H), 1.57-1.25 (m, 10H), 0.85 (s, 3H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 160.8, 151.2, 131.6, 129.9, 125.0, 119.4, 117.6, 114.9, 37.5, 35.4, 35.0, 33.0, 25.7, 21.7, 21.4, 19.5. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{17}H_{19}NO_2Na$, 292.1308; Found: 292.1316.

4-(tert-Butyl)-3-chlorochroman-2-one (**3i**). **Physical state**: White solid; **Yield**: 32.37 mg (68%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.32 (dd, *J* = 9.0, 8.2, 1H), 7.16-7.08 (m, 3H), 5.03 (d, *J* = 5.8 Hz, 1H), 3.18 (d, *J* = 5.7 Hz, 1H), 1.08 (s, 9H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 165.8, 150.6, 130.6, 129.4, 125.1, 124.3, 117.4, 56.8, 52.7, 35.9, 29.5. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{13}H_{15}ClO_2Na$, 261.0653; Found: 261.0655.

Ethyl 4-(tert-butyl)-2-oxochromane-3-carboxylate (**3j**). **Physical state**: Brown gum; **Yield**: 36.47 mg (61%)**. ^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.40 – 7.33 (m, 1H), 7.26 – 7.15 (m, 3H), 4.18 - 4.06 (m, 2H),

4.05 (s, 1H), 3.22 (s, 1H), 1.06 (s, 12H). **$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$)** δ 168.0, 165.9, 151.6, 131.2, 129.0, 124.1, 121.4, 117.0, 62.3, 50.7, 48.7, 34.7, 27.4, 13.9. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{16}H_{20}O_4Na$, 299.1254; Found: 299.1259.

4-(tert-Butyl)-6-methyl-2-oxochromane-3-carbonitrile (**3k**). **Physical state**: White solid; **Yield**: 39.85 mg (82%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.17 (d, *J* = 8.4 Hz, 1H), 7.05- 6.96 (m, 2H), 4.09 (s, 1H), 2.99 (s, 1H), 2.36 (s, 3H), 0.97 (s, 9H). **$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)** δ 160.8, 149.0, 134.8, 131.8, 130.6, 119.4, 117.3, 114.8, 51.5, 35.0, 34.0, 27.30, 20.9. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{15}H_{17}NO_2Na$, 266.1151; Found: 266.1151.

4-((9S,10S)-9,10-Dihydro-9,10-ethanoanthracen-11-yl)-2H-chromen-2-one (**3l**). **Physical state**: White solid; **Yield**: 41.0 mg (55%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.40-7.31 (m, 5H), 7.24 (s, 2H), 7.17 – 7.13 (m, 3H), 6.97 (dd, J = 7.2, 1.8 Hz, 2H), 5.78 (s, 1H), 4.51 (d, *J* = 2.5 Hz, 1H), 4.31 (d, *J* = 1.7 Hz, 1H), 3.63 – 3.59 (m, 1H), 2.94 – 2.89 (m, 1H), 2.07 – 2.01 (m, 1H). **$^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$)** δ 160.61, 148.5, 144.5, 144.1, 143.7, 140.2, 138.0, 128.2, 126.3,125.9, 125.8, 125.1, 125.0, 123.9, 123.8, 123.4, 123.1, 121.2, 117.3, 49.6, 44.6, 38.4, 28.7. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{25}H_{18}O_2Na$, 373.1199; Found: 373.1223.

4-Ethyl-2-oxo-2H-chromene-3-carbonitrile (**4a**). **Physical state**: White solid; **Yield**: 29.85 mg (75%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.88 – 7.68 (m, 2H), 7.43 (t, *J* = 7.8 Hz, 1H), 3.14 (q, *J* = 7.7 Hz, 2H), 1.42 (t, *J* = 7.7 Hz, 3H). **$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$)** δ 168.1, 157.0, 154.0, 135.2, 125.9, 125.6, 118.1, 117.2, 113.3, 101.5, 25.4, 14.1. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{12}H_{10}NO_2$, 200.0706; Found: 200.0717.

2-Oxo-4-propyl-2H-chromene-3-carbonitrile (**4b**). **Physical state**: White solid; **Yield**: 42.17 mg (99%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.76-7.68 (m, 2H), 7.43 – 7.40 (m, 2H), 3.10 (t, *J* = 8.0 Hz, 2H), 1.85-1.79 (m, 2H), 1.16-1.12 (t, *J* = 8.0 Hz, 3H). **$^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$)** δ 166.5, 157.0, 153.9,

135.2, 126.05, 125.5, 118.1, 117.5, 113.5, 102.3, 33.8, 23.4, 14.3. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{13}H_{11}NO_2Na$, 236.0682; Found: 236.0678.

4-Neopentyl-2-oxo-2H-chromene-3-carbonitrile (**4c**). **Physical state**: White solid; **Yield**: 29.88 mg (62%)**. ^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.80 (d, *J* = 7.3 Hz, 1H), 7.71 - 7.66 (m, 1H), 7.41-7.36 (m, 2H), 3.11 (s, 2H), 1.12 (s, 9H). **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)** δ 164.5, 157.0, 153.8, 135.0, 127.7, 124.9, 118.8, 117.9, 114.6, 103.9, 43.65, 35.7, 30.09. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{15}H_{15}NO_2Na$, 264.0995; Found: 264.1020.

4-(But-3-en-1-yl)-2-oxo-2H-chromene-3-carbonitrile **(4d). Physical state**: White solid; **Yield**: 33.23 mg (67%)**. ^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.76 – 7.69 (m, 2H), 7.45 – 7.26 (m, 2H), 5.90 (ddt, *J* = 17.0, 10.5, 6.8 Hz, 1H), 5.11 – 5.07 (m, 2H), 3.21 (t, *J* = 7.8 Hz, 2H), 2.52 (dd, *J* = 15.0, 7.0 Hz, 2H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 165.6, 156.9, 153.8, 135.2, 135.1, 126.0, 125.6, 118.1, 117.6, 117.3, 113.4, 102.2, 33.6, 31.4. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{14}H_{11}NO_2Na$, 248.0681; Found: 248.0682.

2-Oxo-4-(pent-4-yn-1-yl)-2H-chromene-3-carbonitrile (**4e**). **Physical state**: White solid; **Yield**: 29.64 mg (57%)**. ^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.84 (d, *J* = 8.0 Hz, 1H), 7.75-7.68 (m, 1H), 7.45-7.39 (m, 2 H), 3.25 (dd, *J* = 9.2, 7.2 Hz, 2H), 2.44 (td, *J* = 6.6, 2.5 Hz, 2H), 2.14 (dd, *J* = 3.3, 1.8 Hz, 1H), 1.96 (dt, *J* = 16.1, 7.2 Hz, 2H). **^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$)** δ 166.9, 156.5, 153.8, 135.4, 126.0, 125.7, 118.0, 117.3, 113.3, 102.1, 82.5, 70.5, 30.8, 28.3, 18.8. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{15}H_{11}NO_2Na$, 260.0681; Found: 260.0667.

4-Benzyl-2-oxo-2H-chromene-3-carbonitrile (**4f**). **Physical state**: White solid; **Yield**: 33.93 mg (65%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.75 (d, *J* = 8.0 Hz, 1H), 7.65 (t, *J* = 7.8, 1H), 7.40 (t, *J* = 8.2, 1H), 7.36-7.24 (m, 6H), 4.48 (s, 2H). **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)** δ 163.9, 156.9, 154.0, 135.2, 135.0 129.4,

128.3, 127.9, 127.0, 125.5, 118.0, 117.6, 113.7, 103.4, 37.7. **HRMS (ESI/QTOF), m/z:** [M+H]+ Calcd for $C_{17}H_{12}NO_2$, 262.0863; Found: 262.0880.

4-(2-Chlorobenzyl)-2-oxo-2H-chromene-3-carbonitrile (**4g**). **Physical state**: White solid; **Yield**: 33.93 mg (58%) **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.69 – 7.64 (m, 1H), 7.53 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.49 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.41 (dd, *J* = 8.3, 0.6 Hz, 1H), 7.30 – 7.27 (m, 1H), 7.24 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.16 (td, *J* = 7.6, 1.1 Hz, 1H), 6.93 (d, *J* = 7.4 Hz, 1H), 4.60 (s, 2H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 163.1, 156.7, 153.8, 135.3, 133.6, 132.9, 130.3, 129.2, 128.9, 127.7, 126.9, 125.8, 117.9, 117.5, 113.3, 104.5, 35.0. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{17}H_{10}ClNO_2Na$, 318.0292; Found: 318.0295.

4-(4-Bromobenzyl)-2-oxo-2H-chromene-3-carbonitrile (**4h**). **Physical state**: White solid; **Yield**: 38.08 mg (56%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.70 – 7.64 (m, 2H), 7.48 – 7.45 (m, 2H), 7.42 (dd, *J* = 9.0, 1.2 Hz, 1H), 7.36 – 7.31 (m, 1H), 7.16 (d, *J* = 8.5 Hz, 2H), 4.42 (s, 2H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 162.8, 156.6, 154.1, 135.4, 134.0, 132.6, 130.0, 126.7, 125.6, 122.0, 118.1, 117.4, 113.6, 103.6, 37.1. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{17}H_{10}BrNO_2Na$, 361.9787; Found: 361.9802.

4-(Naphthalen-2-ylmethyl)-2-oxo-2H-chromene-3-carbonitrile (**4i**). **Physical state**: White solid; **Yield**: 29 .86 mg (48%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.84 – 7.75 (m, 4H), 7.68-7.61 (m, 2H), 7.51 – 7.45 (m, 2H), 7.41 - 7.38 (m, 2H), 7.30 (d, *J* = 9.0 Hz, 1H), 4.64 (s, 2H). **^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$)** δ 163.4, 156.9, 154.0, 135.2, 133.5, 132.6, 129.3, 127.8, 127.8, 127.1, 127.0, 126.8, 126.5, 126.0, 125.6, 118.0, 117.6, 113.8, 103.51, 37.9. **HRMS (ESI/QTOF), m/z:** [M+K]+ Calcd for $C_{21}H_{13}NO_2K$, 350.0578; Found: 350.0591.

2-Oxo-4-(thiophen-3-ylmethyl)-2H-chromene-3-carbonitrile (**4j**). **Physical state**: White solid; **Yield**: 29.90 mg (56%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.82 (d, *J* = 7.9 Hz, 1H), 7.68 (t, *J* = 7.4 Hz, 1H), 7.42-

7.37 (m, 2H), 7.35 – 7.31 (m, 1H), 7.15 (s, 1H), 7.04 (d, *J* = 6.0 Hz, 1H), 4.46 (s, 2H). **$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$)** δ 163.3, 156.9, 154.0, 135.3, 134.3, 127.4, 127.4, 127.1, 126.7, 125.6, 123.2, 118.0, 117.4, 113.6, 102,7, 32.5. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{15}H_9NO_2SNa$, 290.0246; Found: 290.0245.

4-((1H-Indol-3-yl)methyl)-2-oxo-2H-chromene-3-carbonitrile (**4k**). **Physical state**: White solid; **Yield**: 45.0 mg (75%)**. ^{1}H NMR (300 MHz, DMSO)** δ 11.05 (s, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.73 (t, *J* = 7.9 Hz, 2H), 7.50 (d, *J* = 8.3 Hz, 1H), 7.35 (t, *J* = 7.1 Hz, 2H), 7.20 (d, *J* = 1.5 Hz, 1H), 7.15 – 7.04 (m, 2H), 4.53 (s, 2H). **$^{13}C\{^{1}H\}$ NMR (75 MHz, DMSO)** δ 164.3, 157.1, 153.44, 136.1, 135.1, 127.3, 126.3, 125.2, 124.2, 121.5, 119.0, 118.26, 117.5, 117.2, 114.5, 111.6, 108.9, 102.1, 33.4. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{19}H_{12}N_2O_2Na$, 323.0791; Found: 323.0795.

4-(3-(1H-Indol-3-yl)propyl)-2-oxo-2H-chromene-3-carbonitrile (**4l**). **Physical state**: White solid; **Yield**: 28.21 mg (43%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 11.05 (s, 1H), 7.63-7.59 (m, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.39- 7.35 (M, 1H) 7.34 (dd, *J* = 4.8, 3.6 Hz, 2H),7.22 (t, *J* = 7.3 Hz, 1H), 7.16 (d, *J* = 8.1 Hz, 1H) 7.15-7.06 (m, 2H), 3.15-3.10 (m, 2H), 3.03 (t, *J* = 7.0 Hz, 2H), 2.21-2.17 (m, 2H). **$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$)** δ 167.0, 156.9, 156.7, 153.7, 131.5, 136.0, 127.1, 126.0, 125.4, 122.3, 122.2, 119.5, 118.8, 117.9, 117.3, 114.5, 113.6, 111.4, 101.7, 31.6, 30.6, 25.4. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{21}H_{16}N_2O_2Na$, 351.1104; Found: 351.1107.

tert-Butyl (2-(3-cyano-2-oxo-2H-chromen-4-yl)ethyl)carbamate (**4m**). **Physical state**: White solid; **Yield**: 30.77 mg (49%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.99 (d, *J* = 7.7 Hz, 1H), 7.70 (t, *J* = 7.7 Hz, 1H), 7.43 (dd, *J* = 18.4, 8.1 Hz, 2H), 4.96 (s, 1H), 3.52 (q, *J* = 6.6 Hz, 2H), 3.35 (t, *J* = 6.7 Hz, 2H), 1.42 (s, 9H). **$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$)** δ 163.7, 156.8, 156.1, 153.8, 135.4, 126.5, 125.8, 117.9, 113.6,

102.7, 80.2, 40.2, 32.9, 33.07, 28.4. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{17}H_{18}N_2O_4Na$, 337.1159; Found: 337.1172.

tert-Butyl (3-(3-cyano-2-oxo-2H-chromen-4-yl)propyl)carbamate (**4n**). **Physical state**: White solid; **Yield**: 46.58 mg (71%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.76-7.66 (m, 2H), 7.40 (t, *J* = 1.0 Hz, 2H), 4.94 (s, 1H), 3.31 (d, *J* = 6.2 Hz, 2H), 3.31 (d, *J* = 6.2 Hz, 2H) 3.15 – 3.10 (m, 2H), 1.43 (s, 9H). **^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$)** δ 166.2, 156.8, 156.2, 153.9, 135.9, 126.0, 125.7, 118.1, 117.3, 113.5, 101.9, 79.7, 40.2, 33.8, 30.0, 28.4. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{18}H_{20}N_2O_4Na$, 351.1315; Found: 351.1321.

6-Methyl-2-oxo-4-propyl-2H-chromene-3-carbonitrile **(4o). Physical state**: White solid; **Yield**: 43.13 mg (95%)**. ^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.49 (d, *J* = 9.0 Hz, 2H), 7.30 (d, *J* = 9.0 Hz, 1H), 3.10 – 3.05 (m, 2H), 2.47 (s, 3H), 1.85 – 1.78 (m, 2H), 1.14 (t, *J* = 7.4 Hz, 3H). **^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$)** δ 166.4, 157.2, 152.1, 136.3, 135.4, 125.6, 117.8, 117.2, 113.7, 101.6, 33.7, 23.7, 21.2, 14.3. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{14}H_{13}NO_2Na$, 250.0838; Found: 250.0840.

7-methoxy-2-oxo-4-propyl-2H-chromene-3-carbonitrile **(4p). Physical state**: White solid; **Yield**: 40.33 mg (84%)**. ^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.63 (d, *J* = 9.0 Hz, 1H), 6.95 (dd, *J* = 9.0, 2.5 Hz, 1H), 6.83 (s, 1H), 3.92 (s, 3H), 3.10-2.93 (m, 2H), 1.77 (dt, *J* = 14.9, 7.5 Hz, 2H), 1.11 (t, *J* = 7.3 Hz, 3H)**. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$)** δ 166.4, 165.4, 157.7, 156.2, 127.3, 114.2, 114.0, 111.2, 101.36, 98.1, 56.2, 33.7, 23.5, 14.2. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{14}H_{13}NO_3Na$, 266.0787, Found: 266.0790.

Ethyl 2-oxo-4-propylchromane-3-carboxylate (**4q**). **Physical state**: White solid; **Yield**: 41 mg (72%)**. ^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.31-7.26 (m, 1H), 7.11 – 7.07 (m, 3H), 4.16 – 3.97 (m, 2H), 3.78 (d, *J* = 2.4 Hz, 1H), 3.41 – 3.36 (m, 1H), 1.61 – 1.55 (m, 2H), 1.42 – 1.34 (m, 2H), 1.03 (t, *J* = 7.1 Hz, 3H). 0.94 (t,

J = 7.2 Hz, 3H). **$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$)** δ 167.3, 164.8, 150.8, 128.8, 128.7, 124.7, 124.4, 117.1, 62.2, 52.2, 39.8, 36.6, 19.9, 13.9, 13.8. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{15}H_{18}O_4Na$, 285.1097; Found: 285.1107.

4-(3-(Biphenyl-4-yl)-3-oxopropyl)-2-oxo-2H-chromene-3-carbonitrile **(4r). Physical state**: White solid; **Yield**: 35.37 mg (44%)**. ^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.03 (d, *J* = 8.4 Hz, 2H), 7.85 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.22 - 7.69 (m, 3H), 7.64 – 7.61(m, 2H), 7.49 – 7.41(m, 5H), 3.59 (dd, *J* = 8.4, 6.4 Hz, 2H), 3.47 (t, *J* = 8.0 Hz, 2H). **$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)** δ 195.9, 166.1, 154.0, 146.7, 135.5, 129.1, 128.9, 128.6, 127.6, 127.2, 126.0, 125.8, 118.2, 117.3, 113.41, 102.6, 37.5, 25.9**. HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{25}H_{17}NO_3Na$, 402.1100; Found: 402.1080.

2-Oxo-4-pentadecyl-2H-chromene-3-carbonitrile (**4s**). **Physical state**: White solid; **Yield**: 60.12 mg (79%)**. ^{1}H NMR ($CDCl_3$, 300 MHz**) δ 7.75 – 7.67 (m, 2H). 7.42 (t, *J* = 9 Hz, 2H), 3.12 – 3.07 (m, 2H), 1.80 – 1.70 (m, 2H), 1.52 – 1.47 (m, 2H), 1.25 (m, 22H), 0.87 (t, *J* = 6.6 Hz, 3H)**. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)** δ 166.9, 157.0, 154.0, 135.2, 126.0, 125.6, 118.1, 117.6, 113.5, 101.9, 77.5, 77.2, 76.9, 32.1, 30.1, 29.8, 29.5, 29.4, 22.8, 14.3. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{25}H_{35}NO_2Na$, 404.2560; Found: 404.2546.

(Z)-4-(Heptadec-8-en-1-yl)-2-oxo-2H-chromene-3-carbonitrile (**4t**). **Physical state**: White solid; **Yield**: 56.98 mg (70%)**. ^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.71 (dd, *J* = 15.5, 7.9 Hz, 2H), 7.42 (t, *J* = 6.8 Hz, 2H), 5.35 – 5.34 (m, 2 H), 3.13 – 3.08 (m, 2 H), 2.01 (s, 4 H), 1.77 (dd, *J* = 14.6, 7.1 Hz, 2H), 1.58 – 1.53 (m, 2H), 1.34 (s, 9H), 1.26 (s, 9H), 0.87 (t, *J* = 5.8 Hz, 3H). **$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$)** δ 166.8, 157.0, 153.9, 135.1, 130.2, 129.7, 126.0, 125.5, 118.1, 117.5, 113.5, 101.9, 32.1, 32.0, 30.0, 29.8, 29.7, 29.6, 29.4, 29.2, 29.1, 27.3, 27.2, 22.8, 14.2. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{27}H_{37}NO_2Na$, 430.2717; Found: 430.2723.

4-((1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)methyl)-2-oxo-2H-chromene-3-carbonitrile **(4u). Physical state**: Brown solid; **Yield**: 38.0 mg (44%)**. ^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.86 (d, *J* = 7.9 Hz, 1H), 7.70 – 7.64 (m, 3H) 7.43 (dd, *J* = 14.0, 8.4 Hz, 3H), 7.33 (t, *J* = 7.6 Hz, 1H), 6.84 (d, *J* = 9.0 Hz, 1H), 6.75 (s, 1H), 6.66 (d, *J* = 8.8 Hz, 1H), 5.47 (s, 2H), 3.71 (s, 3H), 2.46 (s, 3H)**. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$)** δ 168.4, 163.6, 153.5, 139.8, 136.3, 135.4, 133.4, 131.5, 130.9, 129.5, 129.3, 126.1, 125.6, 118.1, 115.2, 130.0, 112.0, 100.4, 100.8, 55.7, 33.9, 29.1. **HRMS (ESI/QTOF), m/z:** [M+Na]+ Calcd for $C_{28}H_{19}ClN_2O_4Na$, 505.0925, Found: 505.0921.

2-Oxo-4-((3S)-3-((3S,5R,7S,8S,10R,12R,13S,14R,17S)-3,7,12-trihydroxy-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthren-17-yl)butyl)-2H-chromene-3-carbonitrile (**4v**). **Physical state**: Brown solid; **Yield**: 57.56 mg (54%)**. ^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.69 – 7.60 (m, 2H), 7.38 – 7.20 (m, 2H), 3.89 (s, 1H), 3.79 (s, 1H), 3.48- 3.33 (m, 4H), 3.11 – 3.07 (m, 1H), 2.98 (s, 1H), 2.22 – 2.10 (m, 1H), 1.97 – 1.82 (m, 3H), 1.66 – 1.46 (m, 10H), 1.21 – 1.18 (m, 9H), 0.92 – 0.87 (m, 2H), 0.79 (s, 3H), 0.69 (s, 3H). **^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$)** δ 168.5, 157.2, 153.9, 135.3, 126.1, 125.7, 118.0, 117.5, 113.6, 101.3, 73.2, 72.0, 68.6, 46.6, 45.8, 41.7, 39.8, 39.4, 36.6, 36.4, 35.5, 34.9, 30.5, 29.8, 28.5, 28.2, 27.9, 26.3, 23.5, 22.5, 17.7, 14.3, 12.5. **HRMS (ESI/QTOF), m/z:** [M+K]+ Calcd for $C_{33}H_{43}NO_5K$, 572.2773; Found: 572.2772.

ASSOCIATED CONTENT

The Supporting Information is available free of charge on the ACS Publications website at DOI:

Mechanistic studies, X-ray crystallography data, CIF files, 1H and 13C NMR spectra

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DEDICATION

This work is dedicated to Professor Elias J. Corey on the occasion of his 90th birthday.

REFERENCES

(1) (a) Tellis, J. C.; Primer, D. N.; Molander, G. A. Dual Catalysis. Single-Electron Transmetalation in Organoboron Cross-Coupling by Photoredox/Nickel Dual Catalysis. *Science* **2014**, *345*, 433. (b) Balzani, V.; Bergamini, G.; Ceroni, P. Light: A Very Peculiar Reactant and Product. *Angew. Chem., Int. Ed*. **2015**, *54*, 11320.

(2) (a) Visible Light Photocatalysis in Organic Chemistry (Eds.: Stephenson, C. R. J.; Yoon, T. P.; MacMillan, D. W. C.) Wiley-VCH, Weinheim, **2018**. (b) Wu, J.; Grant, P. S.; Li, X.; Noble, A.; Aggarwal, V. K. Catalyst-Free Deaminative Functionalizations of Primary Amines by Photoinduced Single-Electron Transfer. *Angew. Chem., Int. Ed*. **2019**. (DOI: 10.1002/anie.201814452).

(c) Shaw, M. H.; Twilton, J.; MacMillan, D. W. C. Photoredox Catalysis in Organic Chemistry. *J. Org. Chem*. **2016**, *81*, 6898. (d) Skubi, K. L.; Blum, T. R.; Yoon, T. P. Dual Catalysis Strategies in Photochemical Synthesis. *Chem. Rev*. **2016**, *116*, 10035.

(3) For selected reports on homogenous metal-photoredox catalysts, see: (a) Narayanam, J. M. R.; Stephenson, C. R. J. Visible Light Photoredox Catalysis: Applications in Organic Synthesis. *Chem. Soc. Rev*. **2011**, *40*, 102. (b) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. Visible Light Photoredox Catalysis with Transition Metal Complexes: Applications in Organic Synthesis. *Chem. Rev*. **2013**, *113*, 5322. (c) Hopkinson, M. N.; Tlahuext-Aca, A.; Glorius, F. Merging Visible Light Photoredox and Gold Catalysis. *Acc. Chem. Res*. **2016**, *49*, 2261. (d) Staveness, D.; Bosque, I.; Stephenson, C. R. J. Free Radical Chemistry Enabled by Visible Light-Induced Electron Transfer. *Acc. Chem. Res*. **2016**, *49*, 2295. For reports on dyes, see: (e) Romero, N. A.; Nicewicz, D. A. Organic Photoredox Catalysis. *Chem. Rev*. **2016**, *116*, 10075. For semi-conductor photocatalysts, see: (f) Hagfeldt, A.; Boschloo, G.; Sun, L.; Kloo, L.; Pettersson, H. Dye-Sensitized Solar Cells. *Chem. Rev*. **2010**, *110*, 6595.

(4) (a) Nicewicz, D. A.; Nguyen, T. M. Recent Applications of Organic Dyes as Photoredox Catalysts in Organic Synthesis. *ACS Catal*. **2014**, *4*, 355. (b) Hari, D. P.; Konig, B. Synthetic Applications of Eosin Y in Photoredox Catalysis. *Chem. Commun*. **2014**, *50*, 6688.

(5) (a) Schwarz, J.; Konig, B. Metal-Free, Visible-Light-Mediated, Decarboxylative Alkylation of Biomass-Derived Compounds. *Green Chem.* **2016**, *18*, 4743; and also for the synthesis of NHPI esters **2e**, **2f**, **2j**, **2o**, **2y**, and **2z**. (b) Tlahuext-Aca, A.; Garza-Sanchez, R. A.; Glorius, F. Multicomponent Oxyalkylation of Styrenes Enabled by Hydrogen-Bond-Assisted Photoinduced Electron Transfer. *Angew. Chem., Int. Ed.* **2017**, *56*, 3708. (c) Sandip, M. *N*-(Acyloxy)phthalimides as Redox-Active Esters in Cross-Coupling Reactions. *Adv. Synth. Catal.* **2018**, *360*, 1735. (d) Cao, H.; Jiang, H.; Feng, H., Kwan, J. M. C.; Liu, X.; Wu, J. Photo-induced Decarboxylative Heck-Type Coupling of Unactivated Aliphatic Acids and Terminal Alkenes in the Absence of Sacrificial Hydrogen Acceptors *J. Am. Chem. Soc*. **2018**, *140*, 16360. (e)Zhang, S.; Tan, Z.; Zhang, H.; Liu, J.; Xu, W.; Xu, K. An Ir-photoredox-catalyzed decarboxylative Michael addition of glyoxylic acid acetal as a formyl equivalent. *Chem Commun.* **2017**, *53*, 11642. (f) Ramirez, N. P.; Gonzalez-Gomez, J. C. Decarboxylative Giese-Type Reaction of Carboxylic Acids Promoted by Visible Light: A Sustainable and Photoredox-Neutral Protocol. *Eur. J. Org. Chem.* **2017**, *2017*, 2154.

(6) (a) Zuo, Z.; Cong, H.; Li, W.; Choi, J.; Fu, G. C.; MacMillan, D. W. C. Enantioselective Decarboxylative Arylation of α-Amino Acids via the Merger of Photoredox and Nickel Catalysis. *J. Am. Chem. Soc.* **2016**, *138*, 1832. (b) Wu, X.; Meng, C.; Yuan, X.; Jia, X.; Qian, X.; Ye, J. Transition-Metal-Free Visible-Light Photoredox Catalysis at Room-Temperature for Decarboxylative Fluorination of Aliphatic Carboxylic Acids by Organic Dyes. *Chem. Commun.* **2015**, *51*, 11864. (c) Noble, A.; McCarver, S. J.; MacMillan, D. W. C. Merging Photoredox and Nickel Catalysis: Decarboxylative Cross-Coupling of Carboxylic Acids with Vinyl Halides. *J. Am. Chem. Soc.* **2015**, *137*, 624. (d) Lang, S. B.; O'Nele, K.

M.; Tunge, J. A. Decarboxylative Allylation of Amino Alkanoic Acids and Esters via Dual Catalysis. *J. Am. Chem. Soc.* **2014**, *136*, 1360. (e) H. Huang, G. Zhangand, Y. Chen, Dual Hypervalent Iodine(III) Reagents and Photoredox Catalysis Enable Decarboxylative Ynonylation under Mild Conditions. *Angew. Chem., Int. Ed.*, **2015**, *54*, 7872.

(7) Xue, F.; Wang, F.; Liu, J.; Di, J.; Liao Q.; Lu, H.; Zhu, M.; He, L.; He, H.; Zhang, D.; Song H.; Liu, X. Y.; Qin,Y. A Desulfurative Strategy for the Generation of Alkyl Radicals Enabled by Visible-Light Photoredox Catalysis. *Angew. Chem., Int. Ed.*, **2018**, *57*, 6667. (b) McDonald B. R.; Scheidt K. A. Intermolecular Reductive Couplings of Arylidene Malonates via Lewis Acid/Photoredox Cooperative Catalysis. *Org. Lett*. **2018**, *20*, 6877. (c) Leeuwen T., Buzzetti, L., Perego, L. A.; Melchiorre, P. A Redox-Active Nickel Complex that Acts as an Electron Mediator in Photochemical Giese Reactions. *Angew. Chem., Int. Ed.*, **2019**, *58*, 4953. (d) Miyazawa, K.; Yasu, Y.; Koike, T.; Akita, M. Chem. Commun. Visible-light-induced hydroalkoxymethylation of electron-deficient alkenes by photoredox catalysis. **2013**, *49*, 7249.

(8) (a) Tasior, M.; Kim, D.; Singha, S.; Krzeszewski, M.; Ahn, K. H.; Gryko, D. T. π-Expanded Coumarins: Synthesis, Optical Properties and Applications. *J. Mater. Chem. C*. **2015**, 3, 1421. (b) Skowronski, L.; Krupka, O.; Smokal, V.; Grabowski, A.; Naparty, M.; Derkowaska-Zielinska, B. Optical Properties of Coumarins Containing Copolymers. *Optical Materials.* **2015**, 47, 18. (c) Rabahi, A.; Makhloufi-Chebli, M.; Hamdi, S. M.; Silva, A. M. S.; Kheffache, D.; Boutemeur-Kheddis, B.; Hamdi, M. Synthesis and Optical Properties of Coumarins and Iminocoumarins: Estimation of Ground- and Excited-State Dipole Moments from a Solvatochromic Shift and Theoretical Methods. *J. Mol. Liq*. **2014**, 195, 240. (d) Hadjipavlou-Litina, D.; Kontogiorgis, C.; Pontiki, E.; Dakanali, M.; Akoumianaki, A.; Katerinopoulos, H. E. *J Enzyme Inhib. Med. Chem*. Anti-Inflammatory and Antioxidant Activity of Coumarins Designed as Potential Fluorescent Zinc Sensors. **2007**, *22*, 287. (e) Lv, H.-N.; Wang, S.; Zeng, K.-W.; Li, J.; Guo, X.-Y.; Ferreira, D.; Zjawiony, J. K.; Tu, P.-F.; Jiang, Y. Anti-Inflammatory Coumarin

and Benzocoumarin Derivatives from *Murraya Alata*. *J. Nat. Prod.* **2015**, *78*, 279. (f) Singh, L. R.; Avula, S. R.; Raj, S.; Srivastava, A.; Palnati, G. R.; Tripathi, C. K. M.; Mukesh Pasupuleti, M.; Sashidhara, K. V. Coumarin–Benzimidazole Hybrids as a Potent Antimicrobial Agent: Synthesis and Biological Elevation. *The Journal of Antibiotics*. **2017**, *70*, 954. (g) Emami, S.; Dadashpour, S. Current Developments of Coumarin-Based Anti-Cancer Agents in Medicinal Chemistry. *Eur. J. Med. Chem*. **2015**, *102*, 611.

(9) (a) Min, M.; Kim, Y.; Hong, S. Regioselective Palladium-Catalyzed Olefination of Coumarins via Aerobic Oxidative Heck Reactions. *Chem. Commun.* **2013**, *49*, 196. (b) Zhu, Y.-F.; Wei, Y.-Y. Copper Catalyzed Direct Alkenylation of Simple Alkanes with Styrenes. *Chem. Sci*. **2014**, *5*, 2379. (c) Jafarpour, F.; Hazrati, H.; Mohasselyazdi, N.; Khoobi, M.; Shafiee, A. Palladium Catalyzed Dehydrogenative Arylation of Coumarins: An Unexpected Switch in Regioselectivity. *Chem. Commun*. **2013**, *49*, 10935. (d) She, Z.-J.; Shi, Y.; Cheng, Y.-Y.; Song, F.-J.; You, J.-S. Versatile Palladium-Catalyzed C–H Olefination of (Hetero)arenes at Room Temperature. *Chem. Commun*. **2014**, *50*, 13914. (e) Zhou, S.-L.; Guo, L.-N.; Duan, X.-H. Copper-Catalyzed Regioselective Cross-Dehydrogenative Coupling of Coumarins with Benzylic Csp3–H Bonds. *Eur. J. Org. Chem*. **2014**, *2014*, 8094. (f) Jafarpour, F.; Darvishmolla, M.; Azaddoost, N.; Mohaghegh, F. Direct C-3 alkylation of coumarins via decarboxylative coupling with carboxylic acids. *New J. Chem.*, **2019**,*43,* 9328. (g) Liu, L. X.; Pan, N.; Sheng, W.; Su, L. B.; Liu, L.; Dong, J. Y.; Zhou, Y. B.; Yin, S.-F. Visible Light-Induced Regioselective Decarboxylative Alkylation of the C(sp2)–H Bonds of Non-Aromatic Heterocycles. *Adv. Synth. Catal*., **2019**, *361*, 4126.

(10) (a) Zimmerman, J. R.; Manpadi, M.; Russell, S. Tin-Free Radical Reactions under Minimal Solvent Conditions for the Synthesis of Substituted Chromones and Coumarins. *Green Chem*. **2011**, *13*, 3103. (b) Banerjee, A.; Santra, S. K.; Khatun, N.; Ali, W.; Patel, B. K. Oxidant Controlled Regioselective Mono- and Di-Functionalization Reactions of Coumarins. *Chem. Commun*. **2015**, *51*, 15422.

(11) Jin, C.; Yan, Z.; Sun, B.; Yang, Visible-Light-Induced Regioselective Alkylation of Coumarins via Decarboxylative Coupling with *N*-Hydroxyphthalimide Esters. *Org. Lett*. **2019**. *21*, 2064.

(12) (a) Li, W.; Liu, H.; Jiang, X.; Wang, J. Enantioselective Organocatalytic Conjugate Addition of Nitroalkanes to Electrophilic 2-Iminochromenes. *ACS Catal*. **2012**, *2*, 1535. (b) Deng, H. Y.; Hu, H. B.; Ling, S. Z.; Ferrie, A. M.; Fang, Y. Discovery of Natural Phenols as G Protein-Coupled Receptor-35 (GPR35) Agonists. *ACS Med. Chem. Lett*. **2012**, *3*, 165.

(13) Chen, C. Y.; Zhou, L. Q.; Huang, X.; Liu, W. S. Rapid Detection of Intracellular Cys over Hcy and GSH Using a Novel Two-Photon Coumarinocoumarin-Based Colorimetric and Fluorescent Probe. *J. Mater. Chem. B* **2017**, *5*, 5892.

(14) Chung, K. H.; Kim, J. N.; Ryu, E. K.; Kim K. M. A Facile Synthesis of α-Chloro Enones by Oxidative Chlorination. *Synthesis* **1993**, *3*, 283.

(15) For synthesis of NHPI esters **2a**, **2c**, **2d**, **2g**, and **2m** see: Qin, T.; Cornella, J.; Li, Chao.;. Malins, L. R.; Edwards, J. T.; Kawamura, S.; Maxwell, D. B.; Eastgate, M. D.; Baran, P. S. A General Alkyl-Alkyl Cross-Coupling Enabled by Redox-Active Esters and Alkylzinc Reagents. *Science*., **2016,** *352,* 801.

(16) For synthesis of NHPI esters **2b**, **2h**, and **2n** see: Zheng, C.; Wang, Y.; Xu, Y.; Chen, Z.; Chen, G.; Liang, S. H. Ru-Photoredox-Catalyzed Decarboxylative Oxygenation of Aliphatic Carboxylic Acids Through N-(Acyloxy)Phthalimide. *Org. Lett*. **2018**, *20*, 4824.

(17) For synthesis of NHPI esters **2i**, **2s**, **2x**, and **2za** see: Fawcett, A.; Pradeilles, J.; Wang, Y.; Mutsuga, T.; Myers E. L.; Aggarwal, V. K. Photoinduced Decarboxylative Borylation of Carboxylic Acids. *Science*. **2017***, 357*, 283.

(18) For synthesis of NHPI ester **2k** see: Xu, X.; Sun, J.; Lin, Y.; Cheng, J.; Li, P.; Jiang, X.; Bai, R.; Xie, Y. Iron-Nitrate-Catalyzed Oxidative Esterification of Aldehydes and Alcohols with N-Hydroxyphthalimide: Efficient Synthesis of N-Hydroxyimide Esters. *Eur. J. Org. Chem.* **2017**, 7160.

(19) For synthesis of NHPI ester **2l** see: Huihui, K. M. M.; Caputo, J. A.; Melchor, Z.; Olivares, A. M.; Spiewak, A. M.; Johnson, K. A.; DiBenedetto, T. A.; Kim, S.; Ackerman, L. K. G.; Weix, D. J. Decarboxylative Cross-Electrophile Coupling of NHydroxyphthalimide Esters with Aryl Iodides. *J. Am. Chem. Soc*. **2016**, *138*, 5016.

(20) For synthesis of NHPI ester **2q** see: Hu, C.; Chen Y. Chemoselective and Fast Decarboxylative Allylation by Photoredox Catalysis Under Mild Conditions. *Org. Chem. Front*., **2015***, 2*, 1352.

(21) For synthesis of NHPI ester **2r** see: M. A.; Krylov, I. B.; Hughes, A. M.; Alabugin, I. V.; Nasybullina, D. V.; Sharipov, M. Yu.; Gultyai, V. P.; Terent'ev, A. O. Electrochemical Behavior of N-Oxyphthalimides: Cascades Initiating Selfsustaining Catalytic Reductive N-O Bond Cleavage. *J. Phys. Org. Chem*. **2017**, *30*, e3744.

(22) For synthesis of NHPI ester **2t** see: Pfeiffer, M. J. and. Hanna, S. B. Aminolysis of Activated Esters of Indole-3-acetic Acid in Acetonitrile. *J. Org. Chem*. **1993**, *58*, 735.

(23) For synthesis of NHPI ester **2w** see: Tlahuext-Aca, A.; Candish, L.; Garza-Sanchez, R. A.; Glorius, F. Decarboxylative Olefination of Activated Aliphatic Acids Enabled by Dual Organophotoredox/Copper Catalysis. *ACS Catal*. **2018**, *8,* 1715.

(24) CCDC 1906778 and 1906813 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif.