

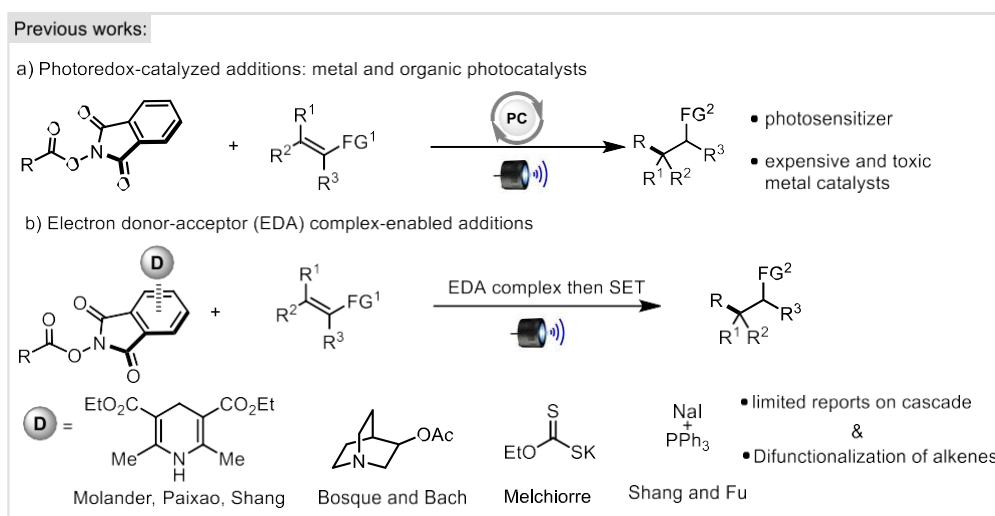
Visible-Light-Driven Radical Cascade with *N*-(Acyloxy)phthalimides: Synthesis of Tetrahydroquinolines through EDA Complex Formation

Research Article:

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2.1 Introduction

Since the last decade, *N*-(acyloxy)phthalimides (NHPI esters) have been extensively utilized as an alternative of Barton esters for the generation of alkyl radicals under thermal, photolytic, or electrochemical conditions.^{116, 119, 190-191} NHPI esters are bench-stable, readily available and can easily be synthesized through coupling of carboxylic acids and *N*-hydroxyphthalimides under standard conditions.^{117, 126, 192} The alkyl radicals generated through extrusion of phthalimide anion and carbon dioxide undergo Giese addition on electronically diverse alkenes under various metallo- and organo-photoredox-catalyzed conditions (Scheme 2.1a).¹⁹⁰ As an alternative to photoredox-catalysis, synthetic methods driven by visible light-induced electron donor-acceptor (EDA) complexes have recently garnered attention.^{21, 193-194} Such methods are cheap, environment friendly, and does not require photocatalysts or oxidants. Accordingly, the research groups of Paixão, Shang, and Molander utilized EDA complex of alkyl NHPI esters and Hantzsch ester (HE, diethyl-1,4-dihydro-2,6-dimethyl-3,5-pyridinedicarboxylate) to generate alkyl radicals that subsequently undergo conjugate addition on a variety of alkenes *via* an overall net-reductive pathway (Scheme 2.1b).^{146, 195-198}

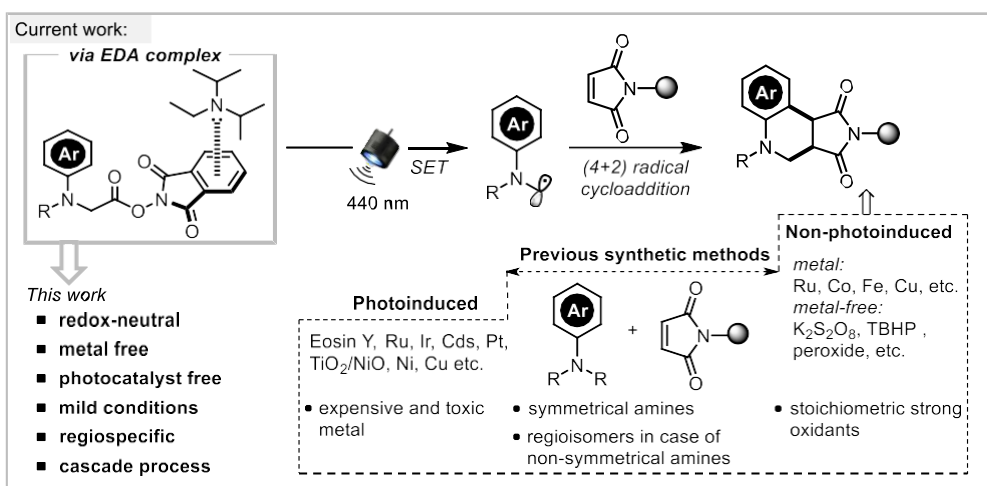


Scheme 2.1 Synthetic Strategies for the Addition of NHPI Esters to Alkenes.

In such EDA-complex photoactivation methods HE serves the role of an electron donor and NHPI acts as an electron acceptor and progenitor of alkyl radical. In a conceptually novel

approach, Shang, Fu and coworkers revealed that a combination of sodium iodide and triphenyl phosphine can serve as a donor in the EDA complex with NHPI esters (Scheme 2.1b).³⁴ Bosque and Bach, and Melchiorre and coworkers demonstrated that quinuclidine and dithiocarbamate, respectively also possess the capability to form an EDA complex with NHPI ester and propel the generated alkyl radical to undergo addition to alkenes.³⁵ Importantly, in all such EDA-complex enabled processes the resulting alkyl radical participate in the mono-functionalization of alkenes through a net-reductive or redox-neutral pathway. The reports concerning EDA-complex driven difunctionalization of alkenes involving NHPI esters that leads to the construction of heterocyclic motifs are scarce.¹⁴⁶

These facts inspired us to examine the feasibility of an EDA-complex promoted cascade between NHPI esters derived from *N*-alkyl-*N*-aryl glycine derivatives and *N*-protected maleimides under metal-free conditions using commercially available and cheap tertiary amines as electron donors. In this envisaged process the α -carbonyl alkyl radical generated through the initial addition of NHPI ester-derived alkyl radical on the maleimides should undergo facile intramolecular homolytic aromatic substitution to afford substituted tetrahydroquinolines that are embedded in many synthetic drugs and natural products.¹⁹⁹⁻²⁰¹ Such a formal (4+2) radical cascade strategy enabling forging of two new C–C bonds through a Csp²–H functionalization would be appealing from the perspective of sustainable synthesis of biologically relevant tetrahydroquinolines. Notably, the prior methods to access such tetrahydroquinolines mostly involved an oxidative annulation between symmetric *N,N*-dialkyl anilines and maleimides under various photochemical conditions using metal-based and organic photosensitizers²⁰²⁻²⁰⁸ as well as under non-photoinduced conditions.²⁰⁹⁻²¹³ Although, some of these reactions employed amicable reaction conditions; most others required either toxic and expensive metal catalysts, elevated reaction temperature or stoichiometric strong oxidants limiting the applicability of such processes.²⁰²⁻²⁰⁴ Furthermore, most of these methods are restricted to symmetric *N,N*-dialkyl anilines, and regioselectivity issues were encountered in case of non-symmetric aniline derivatives.^{209, 211} This thesis includes to develop photoinduced radical cascade strategies involving NHPI esters,²¹⁴⁻²¹⁶ we document an unprecedented EDA-complex photoactivation-driven (4+2) radical annulation between appropriately designed alkyl NHPI esters and *N*-protected maleimides leading to the synthesis of functionally orchestrated tetrahydroquinolines with exclusive regioselectivity (Scheme 2.2).



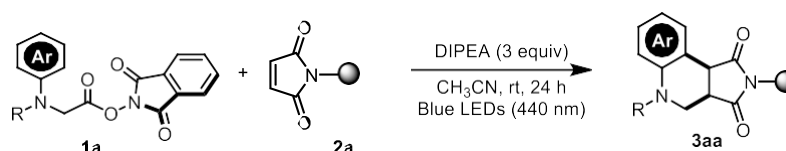
Scheme-2.2 Radical (4+2) Annulation of Alkyl NHPI Esters with *N*-Protected Maleimides.

2.2 Results and Discussion

At the outset, a solution of NHPI ester **1a** (3 equiv), *N*-phenyl maleimide **2a** (1 equiv) and *N,N*-diisopropylethylamine (DIPEA, 3 equiv) in acetonitrile (CH₃CN) was irradiated using blue LEDs (440 nm) at room temperature and under nitrogen atmosphere (Table 1). To our delight,

the reaction went to completion in 24 h and the desired tetrahydroquinoline **3aa** was obtained in 72% yield (entry 1). A quick screening of organic donors, such as DABCO, Hantzsch ester, DMAP, Et₃N, and K₂CO₃ failed to better the yield, and no product formation was observed in case of 2,6-lutidine (entries 2-7). Subsequently, we evaluated different solvents given their crucial role in the formation of EDA complex. Lower yields were obtained in polar aprotic solvents, such as 1,4-dioxane, DMF, DMSO, THF and CH₂Cl₂; and less polar solvents, such as toluene, and protic polar solvents, such as CH₃OH did not support the reaction (entries 8-14). With mixture of solvent such as CH₃CN:HFIP (5:1) also failed to improve the yield (entry 15). Decreasing the amount of NHPI ester **1a** to either 1.5 or 2 equiv had detrimental effects on the outcome of the reaction (entries 16-17). Control experiments revealed the influence of DIPEA loading on the efficacy of the reaction. Decreasing the loading of DIPEA to 1.5 equivalent or carrying out the reaction in the absence of DIPEA caused complete shutdown of reactivity, and increasing the amount to 4 equiv. failed to improve the yield (entries 18-20). Changing the wavelength of light to 427 and 456 nm did not improve the yield (entry 21-22). We then performed the reaction in ambient air instead of a nitrogen atmosphere and tested NHPI ester **1j**, none of which showed any improvement (entry 23-24).

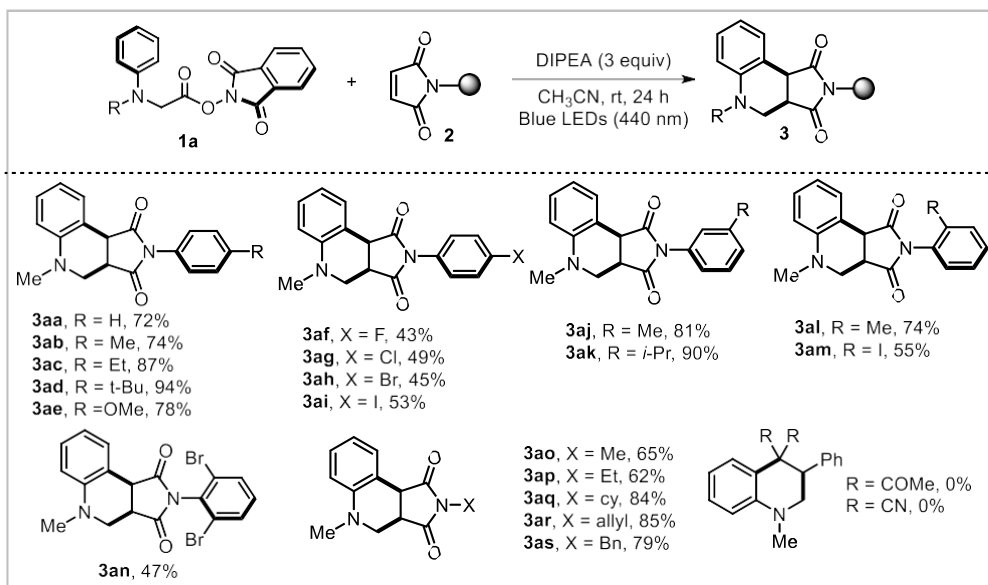
Table 2.1 Optimization of the Reaction Conditions^a



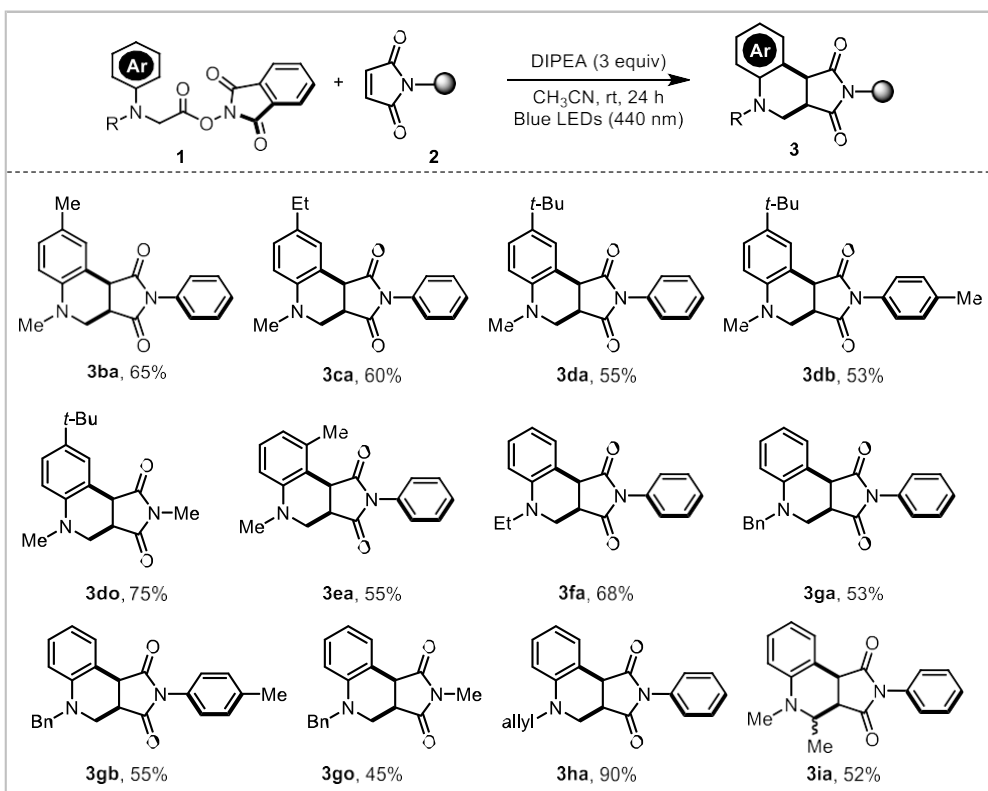
entry	variation from optimized conditions	yield (%) ^b
1	none	72
2	DABCO instead of DIPEA	59
3	Hantzsch ester instead of DIPEA	32
4	DMAP instead of DIPEA	20
5	2,6-lutidine instead of DIPEA	N.D.
6	Et ₃ N instead of DIPEA	68
7	K ₂ CO ₃ instead of DIPEA	42
8	1,4-dioxane instead of CH ₃ CN	61
9	DMF instead of CH ₃ CN	18
10	DMSO instead of CH ₃ CN	N.D.
11	THF instead of CH ₃ CN	68
12	Methanol instead of CH ₃ CN	N.D.
13	CH ₂ Cl ₂ instead of CH ₃ CN	17
14	Toluene instead of CH ₃ CN	N.D.
15	CH ₃ CN:HFIP (5:1) instead of CH ₃ CN	Trace
16	1.5 equiv instead of 3 equiv of 1a	29
17	2 equiv instead of 3 equiv of 1a	42
18	1.5 equiv instead of 3 equiv of DIPEA	N.D.
19	4 equiv instead of 3 equiv of DIPEA	70
20	DIPEA was not used	N.D.
21	Using 427 nm Blue LEDs	55
22	Using 456 nm Blue LEDs	64
23	Without Nitrogen	55
24	Using TCNHPI 1j	35

^aReaction Conditions: **1a** (0.3 mmol), **2a** (0.1 mmol), DIPEA (0.3 mmol), and CH₃CN (1 mL) under Nitrogen atmosphere using Blue LEDs (440 nm) for 24 h. ^bIsolated yield. N.D. = Not Detected.

Next, we explored the scope of the cascade manifold by reacting alkyl NHPI ester **1a** with a variety of *N*-substituted maleimides **2** under optimized conditions (Scheme 2.3). In general, a broad palette of electronically diverse *N*-aryl maleimides exhibited good to excellent reactivity. Diverse electron-rich (Me, Et, *t*-Bu, OMe) and electron-deficient (F, Cl, Br, I) substituents were accommodated at the *para*-position of the phenyl ring in *N*-aryl maleimides to furnish the respective tetrahydroquinoline derivatives (**3ab-3ai**) in moderate to excellent yields (43-94%). Other than *-para*, the *-meta* (3-Me, 3-*i*-Pr) and *-ortho* (2-Me, 2-I, 2,6-di-Br) substitution patterns were well tolerated to afford the corresponding products (**3aj-3an**) in moderate to excellent yields (47-90%).



Scheme 2.3 Scope of *N*-substituted Maleimides.

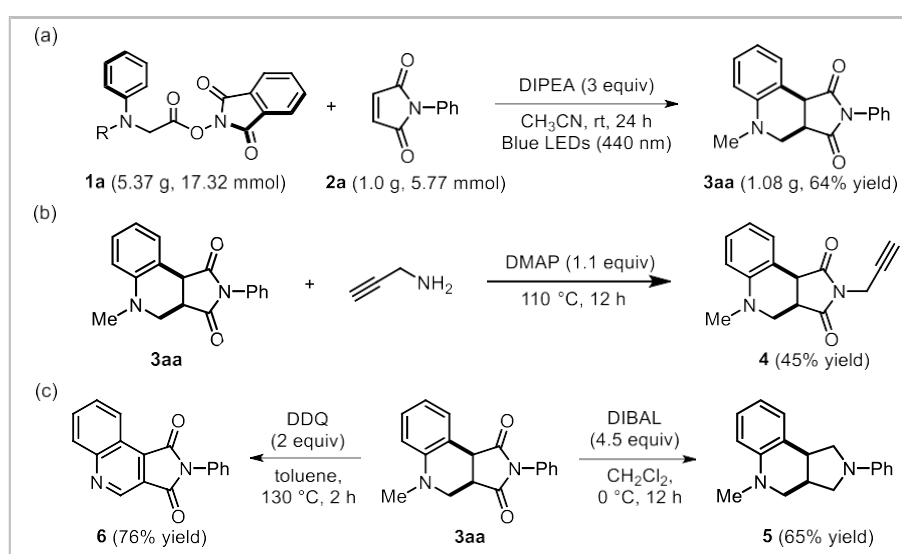


Scheme 2.4 Scope of *N*-(acyloxy)phthalimides.

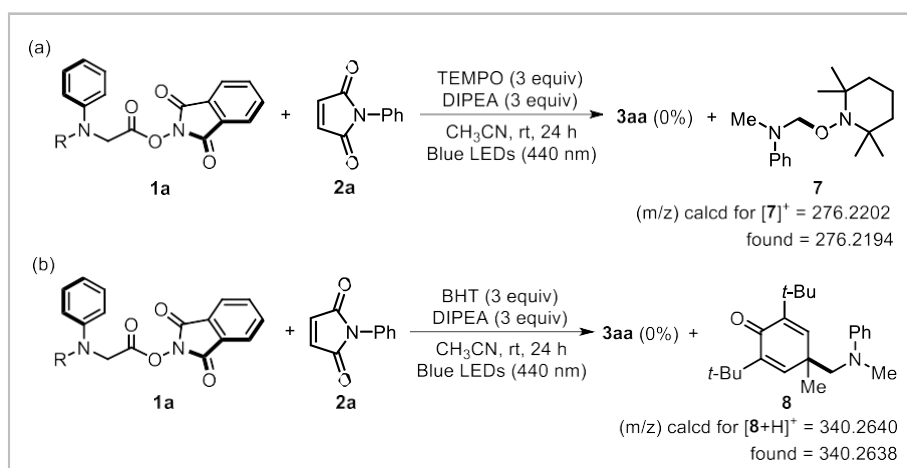
Generally, *N*-aryl maleimides containing electron-rich substituent on the phenyl ring imparted better reactivity as compared to the electron-deficient congeners. Notably, the efficacy of the process was preserved in the case of *N*-alkyl maleimides containing -methyl, -ethyl, -cyclohexyl, -allyl, and -benzyl moieties as *N*-substituents to give the desired products (**3ao–3as**) in good yields (62–85%). Unfortunately, Michael acceptors other than maleimides proved inefficient under the current protocol.

Subsequently, we investigated the scope of alkyl NHPI ester **1** by varying the electronic and substitution pattern on the *N*-aryl ring (Scheme 2.4). NHPI esters containing unsubstituted phenyl ring as well as arene rings embedded with electron-rich substituents (4-Me, 4-Et, 4-*t*-Bu) reacted with both *N*-aryl and *N*-methyl maleimides to furnish the corresponding products (**3aa–3da**, **3db**, **3do**) in good yields (53–75%). Interestingly, NHPI ester having 3-Me substituted phenyl ring underwent planned tandem process to provide the desired product **3ea** (55%) in a regioisomerically pure form. Unfortunately, no product formation was observed in case of *ortho*-substituted *N*-aryl glycinate substrates, which could be attributed to steric effect.²⁰⁴ Moreover, we also explored the scope of the reaction with regard to different *N*-protecting groups. The reaction was found to be tolerated to the presence of several *N*-alkyl substituents, such as ethyl, benzyl and allyl to afford the desired products (**3fa–3ga**, **3gb**, **3go**, **3ha**) in moderate to excellent yields (45–90%). Other than primary, secondary alkyl NHPI ester also delivered the expected radical cyclization product **3ia** in 52% yield. It is noteworthy that compounds, such as **3ia** could not be prepared by earlier methods as in case of non-symmetrical *N,N*-dialkyl anilines, either regioisomeric mixtures were obtained or generation of aminoalkyl radical and subsequent C-C bond formation took place exclusively on the *N*-methyl carbon.^{205, 209, 211} Unfortunately, heteroaryl substitution on either the *N*-aryl glycinate derived NHPI ester or maleimide could not be accommodated.

The scalability of the method was demonstrated by reacting 1 g of *N*-phenyl maleimide **2a** with **1a** to furnish the desired product **3aa** in 64% yield (Scheme 2.5a). Importantly, the final products were amenable for further synthetic manipulation. Accordingly, **3aa** was successfully subjected to transimidation in the presence of propargyl amine to give **4** in 45% yield (Scheme 2.5b). Moreover, **3aa** was reduced by an excess of DIBAL to the corresponding pyrrolidine derivative **5** in 65% yield, and oxidized in the presence of DDQ to afford the respective quinoline scaffold **6** in 76% yield (Scheme 2.5c).



Scheme 2.5 Scale up Experiment and Post-synthetic Modifications.



Scheme 2.6 Control Experiments.

The radical intermediacy in these transformations were probed through reacting **1a** and **2a** in the presence of TEMPO (2,2,6,6-tetramethyl-1-piperidine-1-oxyl) and BHT (2,6-di-*tert*-butyl-4-methylphenol) as radical scavengers (Scheme 2.6). In both these cases formation of **3aa** was not observed, and corresponding TEMPO and BHT adducts **7** and **8** were detected by high-resolution mass spectrometry. These experiments unequivocally established the intermediacy of alkyl radicals in these processes.

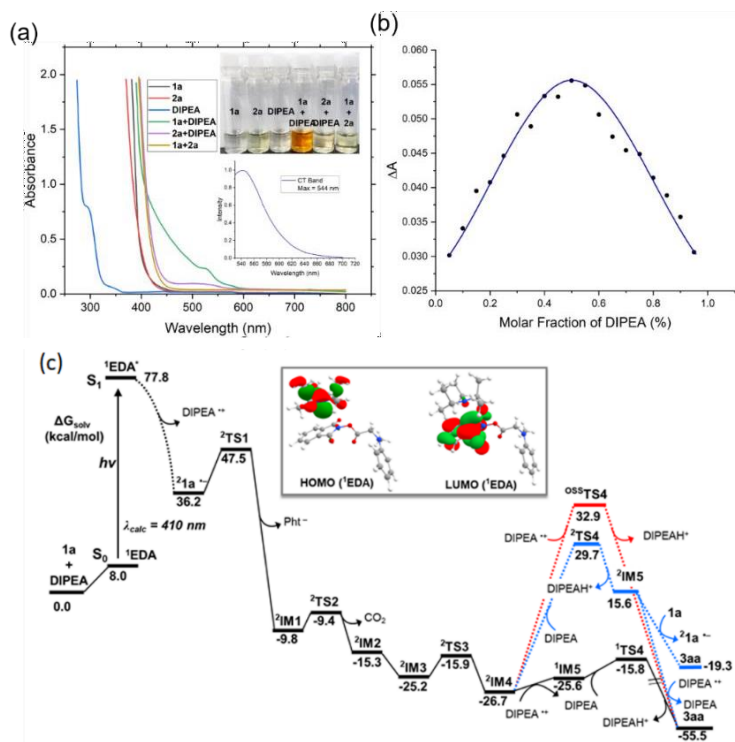
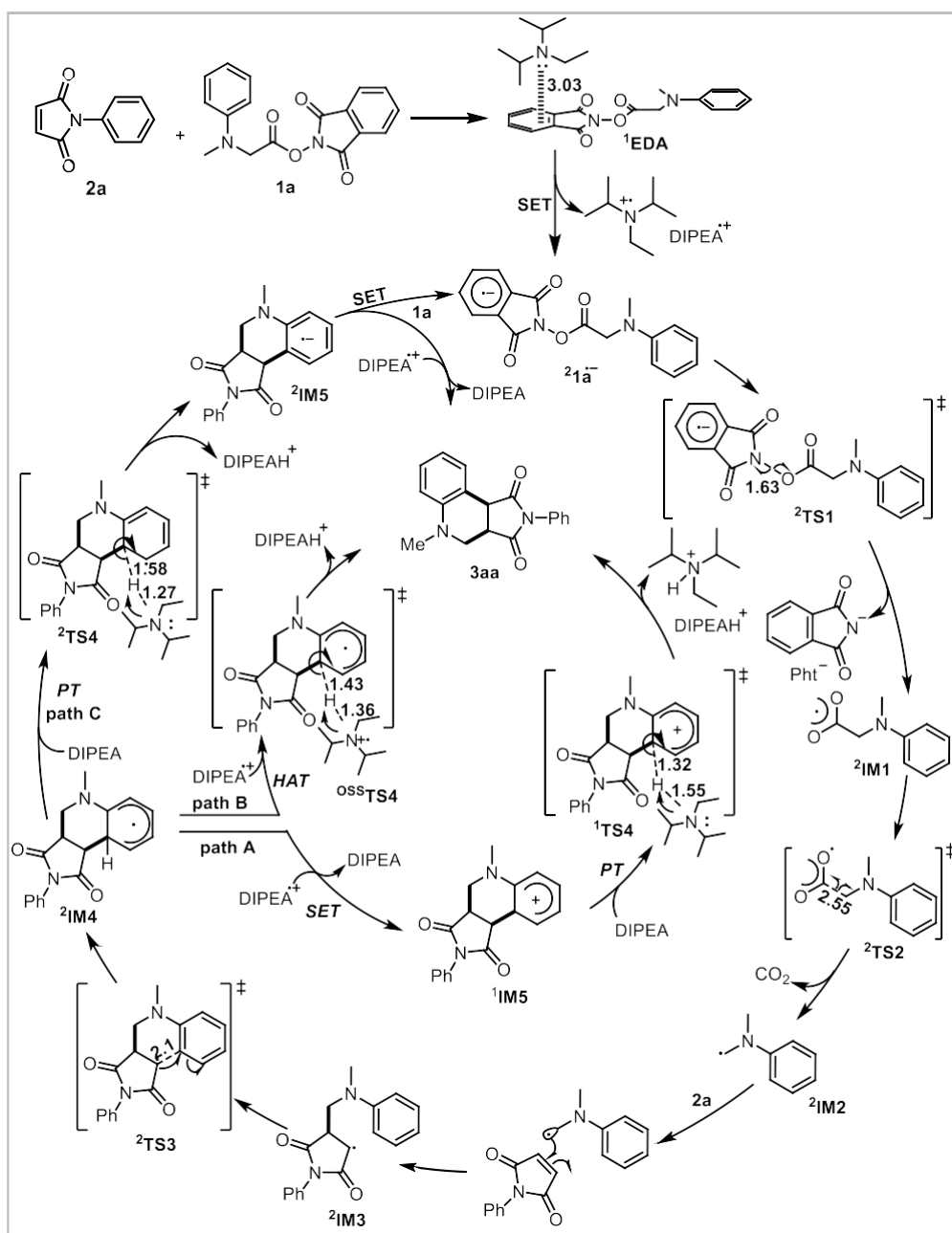


Figure 2.1 (a) UV-vis absorption spectra of **1a** (0.3 M), **2a** (0.1 M), and DIPEA (0.3 M). (b) Job's plot between **1a** and DIPEA at 440 nm. (c) Relative Gibbs free energy profile at B3LYP-D3(BJ)/SMD(MeCN)/6-311+G(d,p) in kcal/mol for the reaction of **1a**, **2a** and DIPEA in acetonitrile. Black, red and blue profiles represent paths A, B and C respectively. Inset: Plots of HOMO and LUMO of ¹EDA complex. Color code: C(grey), N(blue), H(white), O(red).

To get insight into the reaction mechanism and provide evidence for the formation of EDA aggregation, ultraviolet/visible (UV-Vis) absorption spectrum of individual reaction partners as well as that of combined reaction components were recorded. After mixing alkyl NHPI ester **1a** and DIPEA, the solution developed a dark yellow color, and its absorption

spectrum clearly depicted a bathochromic displacement in the visible region, indicative of the formation of a charge-transfer molecular aggregate (Figure 2.1a). In contrast, no EDA complex formation was observed when maleimide **2a** was mixed with either **1a** or DIPEA. Additionally, Job's plot analysis of this complex showed a maximal absorbance at 50% molar fraction of DIPEA, which indicated a stoichiometry of 1:1 between NHPI ester **1a** and DIPEA in the EDA complex (Figure 2.1b).

Next, we conducted density functional theory (DFT) and time-dependent DFT (TD-DFT) calculations at B3LYP-D3(BJ)/SMD(MeCN)/6-311+G(d,p) and CAM-B3LYP-D3(BJ)/SMD(MeCN)/6-311+G(d,p),²¹⁷ respectively, to get insight into the reaction mechanism (Figure 2.1c). A general mechanistic picture is shown in Scheme 2.7, considering the reaction of **1a** with **2a** in the presence of DIPEA (Table 1, entry 1).²¹⁸



Scheme 2.7 Proposed Mechanism.

The binding of DIPEA to **1a** results in the formation of an EDA complex (**1EDA**) via lp- π stacking interaction between the amine and the phthalimide moiety, at an interatomic distance

of 3.03 Å (Scheme 2.7) and $\Delta G = 8.0$ kcal/mol (Figure 2.1c). As shown in Figure 2.1c (inset), the HOMO of **1EDA** is N *p*-orbital based, while the LUMO has significant contribution from π^* of phthalimide. **1EDA** constitutes the photoactive S_0 species and undergoes photoexcitation to the S_1 complex, **1EDA***, at a predicted absorption wavelength, $\lambda_{\text{calc}} = 410$ nm (Figure 2.1c), in agreement to experiments ($\lambda_{\text{max}} = 440$ nm). This results in disintegration of the singlet excited **1EDA*** to radical anionic doublet species **21a^{-•}** and radical cationic DIPEA^{•+}. **21a^{-•}** features a single electron occupancy on the phthalimide π^* , rationalizing charge transfer from the donor to the acceptor of the light-responsive complex. Subsequently, **21a^{-•}** undergoes N–O bond cleavage overcoming an intrinsic reaction barrier of 11.3 kcal/mol ($\Delta G^\ddagger = 47.5$ kcal/mol with regard to the separated reactants) through **2TS1** (Figure 2.1c), followed by removal of phthalimide anion (Pht⁻) to generate **2IM1**. Interestingly, this resulting intermediate features a radical (CO₂)[•] unit, facilitating decarboxylation and transformation to **2IM2** in an essentially barrier-less process (**2TS2**, $\Delta G^\ddagger = 0.4$ kcal/mol, Figure 1c).²¹⁵ Thereafter, the C-radical on **2IM2** readily carries out an electrophilic addition on the olefinic group of maleimide **2a** to afford radical intermediate **2IM3**. Incidentally, calculations reveal that a radical coupling between TEMPO and **2IM2** leading to **7** ($\Delta G = -12.6$ kcal/mol) is thermodynamically more feasible than generation of **2IM3** ($\Delta G = -9.9$ kcal/mol), curtailing the possibility of the proposed reaction cycle and target product formation. Nevertheless, in absence of any radical scavenger, subsequent intramolecular radical cyclization through **2TS3** at an intrinsic energetic expense of 9.3 kcal/mol leads to the formation of a stable radical intermediate **2IM4**.²¹⁹

From here, we envisaged three possible pathways (A, B and C) enroute to the final product **3aa** (Scheme 2.7). Path A constitutes a single electron transfer (SET) from **2IM4** to DIPEA^{•+} to form a cationic intermediate **1IM5** and neutral DIPEA on the singlet surface. This is followed by a facile proton abstraction by DIPEA to achieve re-aromatization through **1TS4** ($\Delta G^\ddagger = 10.9$ kcal/mol) and furnish the targeted tetrahydroquinoline, **3aa**. Two alternate pathways, namely, Path B (red arrows) and C occurs on the open-shell singlet and doublet surface, respectively. Path B features a concerted H-atom transfer (HAT) by DIPEA^{•+} while path C consists of sequential proton transfer (PT)/SET to a DIPEA/DIPEA^{•+} pair, respectively. We ruled out the possibility of path B and C due to predominantly higher energetic requirement (~56 – 60 kcal/mol). These computational findings are in concurrence with the results of “light/dark” experiment and quantum yield measurement. The “light/dark” experiment revealed the necessity of constant irradiation for the formation of **3aa**, and quantum yield ($\Phi = 3.4$) suggested shorter chain lengths; hence, ruling out the possibility of a radical chain mechanism (path C) as the dominant pathway.

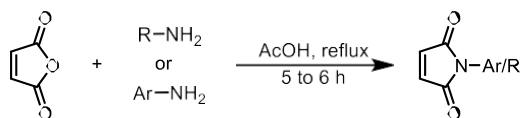
2.3 Experimental Section

2.3.1 General Information

Photoredox reactions were performed under a N₂ atmosphere for all the reaction sets using predried glassware and standard Schlenk tubes. All the solvents were obtained from Merck (Emparta grade) and were dried with calcium hydride and freshly distilled under Nitrogen. The following starting materials and the reaction components *N*-phenyl, methyl and ethyl maleimides, *N*-hydroxyphthalimide, maleic anhydride, All substituted anilines, α -bromoacetic acid, *N,N'*-Dicyclohexylcarbodiimide (DCC), 4-*N,N*-dimethylamino-pyridine (DMAP), NaH, DIPEA, BHT and TEMPO were obtained from commercial sources and used without further purification. Other maleimides and phthalimide ester derivatives were synthesized by the synthetic procedures mentioned below. Yields refer to isolated compounds, estimated to be >95% pure as determined by ¹H NMR and ¹³C NMR. All optimized reactions were conducted under the photo irradiation using 40W Kessil blue LED (440 nm) lamp. Thin layer chromatography (TLC) was performed on Merck pre-coated silica gel 60 F254 aluminum sheets with detection under UV light at 254 nm. Chromatographic separations were carried out

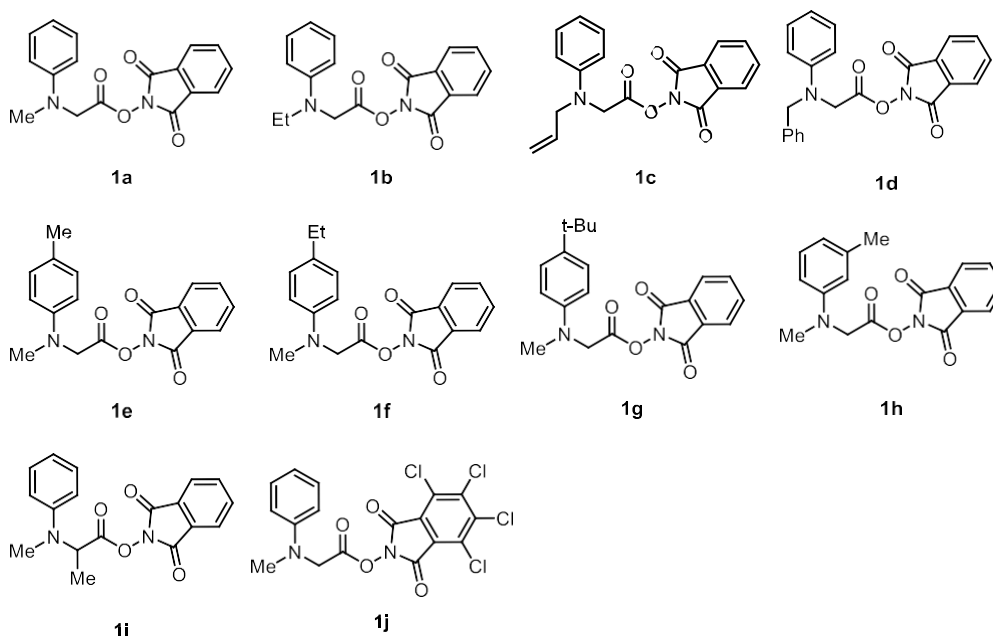
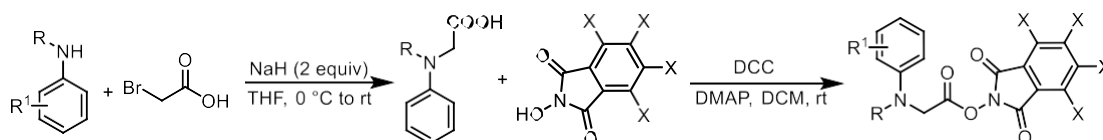
on Avra silica gel (100-200 mesh or 230-400 mesh). Nuclear magnetic resonance (NMR) spectroscopy was performed using Bruker 500 MHz spectrometers. If not otherwise specified, chemical shifts (δ) are provided in ppm. HRMS spectra were recorded using Agilent 6500 Q-TOF spectrometer. UV experiment was performed on LABINDIA ANALYTICAL-2000 U UV/VIS Spectrophotometer instrument.

2.3.2 General Procedure (GP) for the Synthesis of Maleimides



To a stirred solution of maleic anhydride (2.45 gm, 25 mmol, 2.5 equiv) in acetic acid (15 mL) was added the amine (10 mmol, 1 equiv). The reaction mixture was stirred at reflux for 6 h (oil bath), and then the acetic acid was removed in vacuo. The residue was dissolved in CH_2Cl_2 (20 mL) and washed with aqueous NaHCO_3 (2×30 mL), HCl (1 M, 2×30 mL), and saturated aqueous NaCl (30 mL). The organic layer was separated, dried over Na_2SO_4 , and the solvent was removed in vacuo. Crude maleimides **2** were further purified by silica gel column chromatography using 20% ethylacetate in hexane as the eluent to obtain pure maleimides **2**.

2.3.3 General Procedure (GP) for the Preparation of NHPI Esters



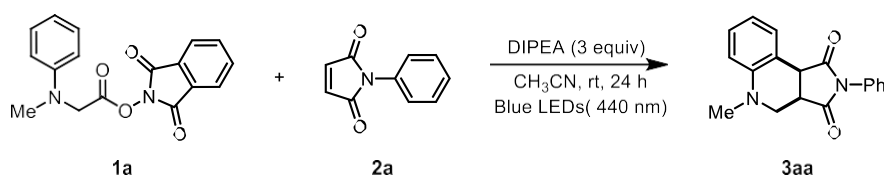
General Procedure Step A: An oven dried 250 mL round bottom flask was equipped with a magnetic stir bar and a reflux condenser. Sodium hydride (0.8 g, 60% dispersion in mineral oil, 20 mmol, 2 equiv) was then suspended in dry THF (20 mL) at 0 °C under nitrogen. A solution of *N*-substituted aniline derivatives (10 mmol) in dry THF (30 mL) was then added slowly. After 30 min, bromoacetic acid (1.39 gm, 10 mmol, 1 equiv) dissolved in dry THF (30 mL) was added drop wise. The mixture was heated to reflux, and the progress of the reaction was monitored by TLC. Upon completion, the mixture was cooled down to room temperature and diluted with

water (60 mL). The reaction mixture was extracted with EtOAc (2 x 30 mL), the aqueous layer was acidified with HCl (2 M) until pH 2 was reached and extracted with EtOAc (3 x 30 mL). The combined organic layers were dried over Na₂SO₄, and the solvent was removed under reduced pressure to give substituted glycine derivatives, which were used in the next step without further purification.

General Procedure Step B: *N*-Hydroxyphthalimide or *N*-Hydroxytetrachlorophthalimide (1.0 eq), DMAP (0.1 eq) and substituted glycine (1.0 eq) was added to a round-bottomed flask. Dichloromethane (0.1 M) and carboxylic acid (1.0 eq) were then added, followed by DCC or DIC (1.0 eq.). The reaction mixture was then allowed to stir at room temperature overnight, before concentrating under reduced pressure. The crude residue was directly purified by silica gel flash-column chromatography (Hexane with EtOAc) to yield pure alkyl NHPI esters **1a** to **1i**. If solid and not pure, the NHPI esters can be recrystallized from DCM/MeOH or EtOAc to give pure material.

2.3.4 Representative General Procedure (GP-1) for the Visible Light-Mediated Photoredox-Catalyzed Reaction

1-Phenyl-1*H*-pyrrole-2,5-dione **2a** (0.043 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-phenylglycinate **1a** (0.232 g, 0.75 mmol, 3 equiv) and DIPEA (130.6 μ L, 0.75 mmol, 3 equiv) were added in a pre-dried 10 ml Schlenk tube under N₂ atmosphere. The tube was degassed and purged with N₂ three times. Then dry acetonitrile (2.5 mL) was added under the N₂ atmosphere. The resulting reaction mixture was allowed to stir for 24 h at room temperature under the irradiation of 40 W Kessil blue LED (440 nm) lamp. After completion (24 h), the reaction mixture was concentrated under vacuum, and purified by silica gel column chromatography using 20% ethyl acetate in hexane to afford the desired product **3aa**.



2.3.5 Image of the photoinduced reaction setup

Front view:



Top view:

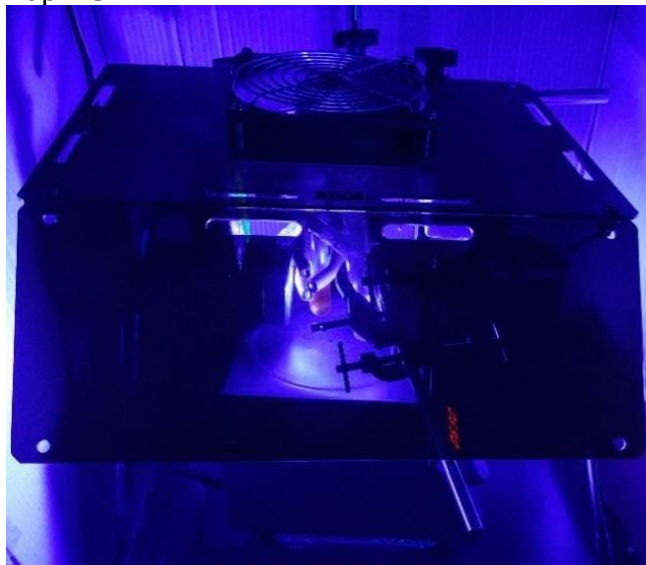


Figure 2.2 Representative Pictures of Reaction Setup.

2.3.6 Control Experiment

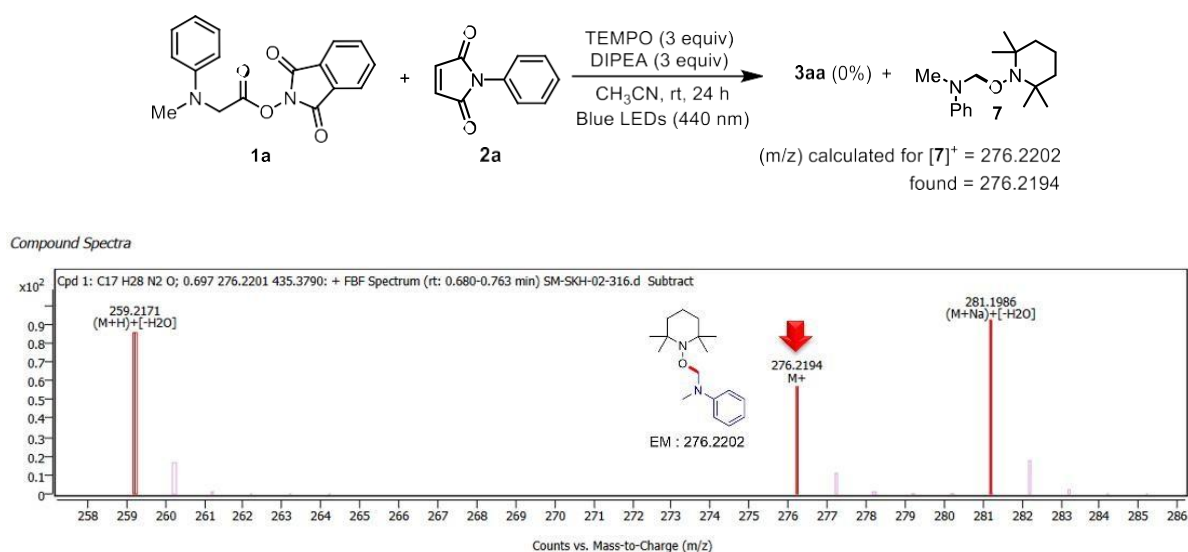


Figure 2.3 HRMS Data of TEMPO Adduct.

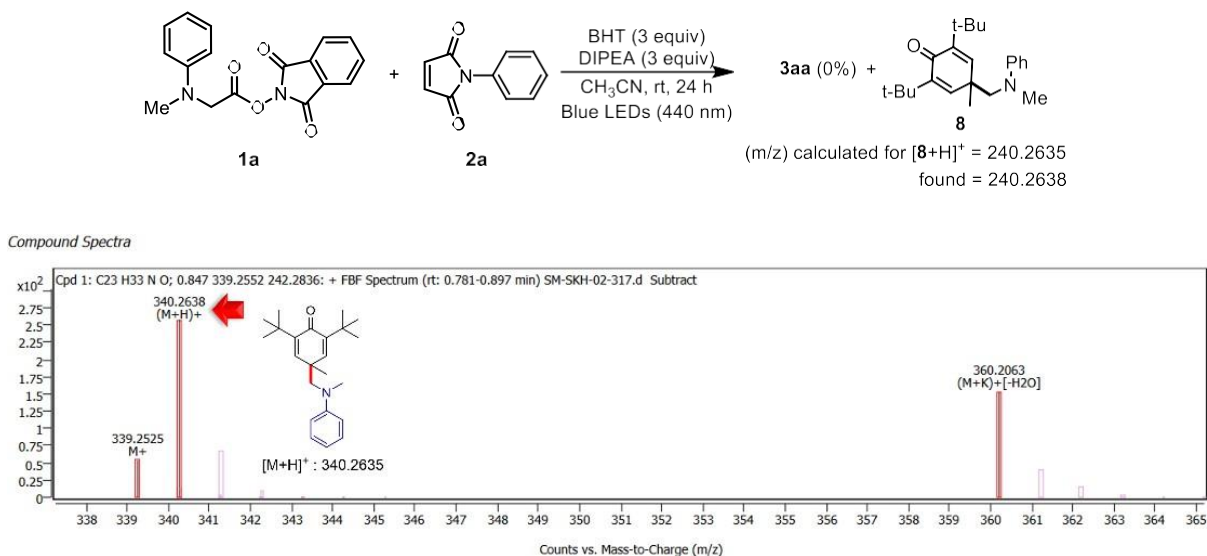


Figure 2.4 HRMS Data of BHT Adduct.

2.3.6 Light- Dark Experiment

1-Phenyl-1*H*-pyrrole-2,5-dione 2a (0.052 g, 0.3 mmol), 1,3-Dioxoisindolin-2-yl *N*-Methyl-*N*-phenylglycinate 1a (0.279 g, 0.9 mmol) and DIPEA (156.7 μ L, 0.9 mmol) were added in a pre-dried 10 ml Schlenk tube under N₂ atmosphere. The tube was degassed and purged with N₂ three times. Then dry acetonitrile (3 ml) was added under the N₂ atmosphere. The mixture was irradiated using a 40 W Kessil blue LED (440 nm) lamp and the reaction was placed in light and dark in every alternative 2 hour. After every time interval of 2 hour, a 0.5 ml reaction aliquot was taken out by a syringe and quenched with water, organic part was taken in ethyl acetate and NMR was carried out. The NMR yield was determined using mesitylene as an internal standard.

Table 2.2 NMR yield with different time

Entry	Time(h)	Light source	Yield (%)
1	2	on	45
2	4	off	45
3	6	on	48
4	8	off	48
5	10	on	51
6	12	off	51

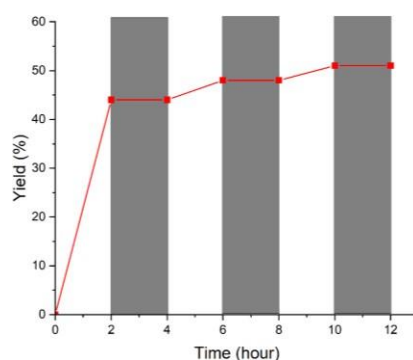


Figure 2.5 Light- Dark Experiment.

2.3.7 Determination of Quantum Yield

(a) Determination of light intensity of the Blue LED:

The photon flux was determined by using standard ferrioxalate actinometry.⁷ A 0.15 M solution of ferrioxalate was made by mixing 737 mg of potassium ferrioxalate hydrate in 10 mL of 0.05 M H₂SO₄. A buffered solution of phenanthroline was made by mixing 25 mg of phenanthroline and 5.63 g of sodium acetate in 25 mL of 0.5 M H₂SO₄. Both solutions were kept in the dark. To determine the photon flux, 1.0 mL of the ferrioxalate solution was placed in a cuvette and irradiated for 60.0 seconds at $\lambda = 440$ nm placing 8 cm away from 40 W Kessil blue LED lamp. After irradiation, 0.175 mL of the phenanthroline solution was added to the cuvette. The solution was then kept for 1 h to permit the ferrous ions to completely coordinate to the phenanthroline. The absorbance of the solution was determined at 510 nm. A non-irradiated sample was also prepared and the absorbance at 510 nm was determined. Conversion was calculated using eq. 1

$$\text{mol Fe}^{2+} = \frac{V \cdot \Delta A}{\epsilon \cdot l} \dots\dots\dots 1$$

Where V is the total volume (0.001175 L) of the solution after addition of the phenanthroline, ΔA is the difference in absorbance at 510 nm between the irradiated and non-irradiated solutions, l is the path length (1.000 cm), and ϵ is the molar absorptivity at 510 nm (11,100 L mol⁻¹ cm⁻¹).

$$\text{mol Fe}^{2+} = \frac{0.001175 \text{ L. (0.7099-0.3663)}}{1 \text{ cm } 11100 \text{ L.cm}^{-1} . \text{mol}^{-1}}$$

$$= 7.2 \times 10^{-8} \text{ mol}$$

The photon flux can be calculated using eq 2.

$$\text{photon flux} = \frac{\text{mol Fe}^{2+}}{\Phi \cdot t \cdot f} \dots\dots\dots 2$$

Where Φ is the quantum yield for the ferrioxalate actinometer (1.01 for a 0.15 M solution at $\lambda = 440 \text{ nm}$), t is the time (60 s), and f is the fraction of light absorbed at $\lambda = 440 \text{ nm}$, $f = 1.000 - 10^{-A}$.
Calculated $f = 1.000 - 10^{-A} = 1.000 - 10^{-0.3436} = 0.805$

$$\text{photon flux} = \frac{7.2 \times 10^{-8} \text{ mol}}{1.01 \times 60 \text{ s} \times 0.805} = 14.76 \times 10^{-10} \text{ Einstein s}^{-1}$$

(B) Quantum Yield Calculation

1-Phenyl-1*H*-pyrrole-2,5-dione **2a** (0.043 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-phenylglycinate **1a** (0.232 g, 0.75 mmol) and DIPEA (130.6 μL , 0.75 mmol), were added in a pre-dried 10 ml schlenk tube under N_2 atmosphere. The tube was degassed and purged with N_2 three times. Then dry acetonitrile (2.5 ml) were added under the N_2 atmosphere. The mixture was irradiated using a 40 W Kessil blue LED (440 nm) lamp and the reaction was placed in light and dark in every alternative 2 hour. After every time interval of 2 hour the reaction aliquot was taken out 1 ml by a syringe and quenched with water, organic part taken in ethylacetate and NMR was carried out. The yield was determined using dichloromethane as NMR standard.

The quantum yield was calculated as follows:

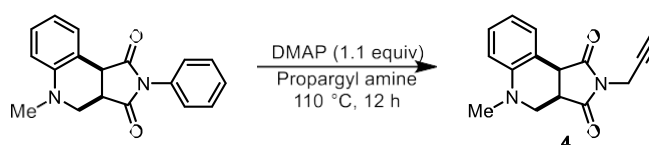
$$\Phi = \frac{\text{mol product}}{\text{flux} \cdot t \cdot f}$$

Where, flux is the photon flux determined by ferrioxalate actinometry ($7.679 \times 10^{-10} \text{ Einstein/s}$), t is the time (7200 s), and f (> 0.999) is the fraction of light absorbed by eosin Y at 440 nm under the reaction condition mentioned above.

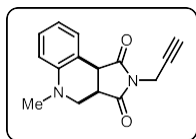
$$\Phi = \frac{3.7 \times 10^{-5}}{14.76 \times 10^{-10} \times 7200 \times 1}$$

$$= 3.4$$

2.3.8 Post Synthetic Modifications

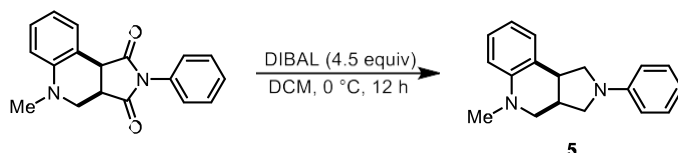


5-Methyl-2-(prop-2-yn-1-yl)-3a,4,5,9b-tetrahydro-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (4)

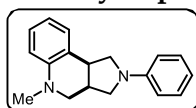


3aa (80 mg, 0.26 mmol) and DMAP (35 mg, 0.29 mmol, 1.1 equiv) were dissolved in propargyl amine (2.6 mL) at room temperature. The mixture was heated at 110 °C, and then stirred for 12 h. After cooling to ambient temperature, silica gel column chromatography of the crude mixture provided the transimidation product **4** (0.011 g, 45% yield).

^1H NMR (500 MHz, CDCl_3) δ 7.48 (d, J = 7.4 Hz, 1H), 7.25 – 7.19 (m, 1H), 6.90 (td, J = 7.5, 1.0 Hz, 1H), 6.71 (d, J = 8.0 Hz, 1H), 4.24 (qd, J = 17.0, 2.5 Hz, 2H), 4.05 (d, J = 9.5 Hz, 1H), 3.52 (dd, J = 11.5, 2.7 Hz, 1H), 3.42 (ddd, J = 9.5, 4.5, 2.7 Hz, 1H), 3.06 (dd, J = 11.5, 4.5 Hz, 1H), 2.79 (s, 3H), 2.17 (t, J = 2.5 Hz, 1H). ^{13}C NMR (126 MHz, CDCl_3) δ 177.3, 175.4, 148.5, 130.3, 128.8, 119.8, 118.4, 112.6, 76.6, 71.6, 50.5, 43.7, 42.1, 39.5, 28.3. HRMS-ESI (m/z): calcd for $\text{C}_{15}\text{H}_{15}\text{N}_2\text{O}_2$ [$\text{M}+\text{H}$] $^+$ 255.1128; found 255.1130.

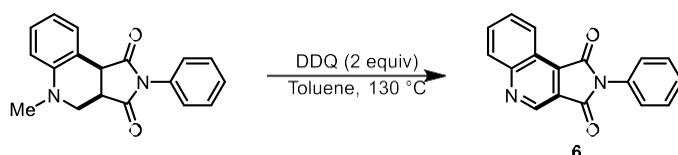


5-Methyl-2-phenyl-2,3,3a,4,5,9b-hexahydro-1H-pyrrolo[3,4-c]quinoline (**5**)

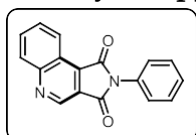


DIBAL (1 M solution in DCM, 0.45 mL, 0.45 mmol, 4.5 equiv) was slowly added to a solution of **3aa** (31 mg, 0.1 mmol) in DCM (1 mL) at 0 °C. After stirring for 12 h, the mixture was diluted by ethyl acetate and washed by saturated NH_4Cl aqueous solution. The organic layer was dried with MgSO_4 , and filtered, concentrated under the vacuum, and purified through flash column chromatography to give the desired product **5** (0.017 g, 65% yield).

^1H NMR (500 MHz, CDCl_3) δ 7.25 (dd, J = 8.5, 7.4 Hz, 2H), 7.20 – 7.13 (m, 2H), 6.77 – 6.68 (m, 3H), 6.57 (d, J = 7.9 Hz, 2H), 3.84 (t, J = 8.8 Hz, 1H), 3.73 (dd, J = 9.6, 6.6 Hz, 1H), 3.58 (dd, J = 15.9, 8.5 Hz, 1H), 3.24 (t, J = 9.2 Hz, 1H), 3.19 (dd, J = 9.6, 1.9 Hz, 1H), 3.13 (dd, J = 11.4, 4.9 Hz, 1H), 3.02 (s, 1H), 2.93 (s, 3H), 2.85 – 2.77 (m, 1H). ^{13}C NMR (126 MHz, CDCl_3) δ 147.7, 146.4, 129.6, 129.3, 127.7, 123.5, 117.1, 115.8, 111.9, 111.7, 54.9, 52.0, 51.9, 39.6, 39.6, 35.1. HRMS-ESI (m/z): calcd for $\text{C}_{18}\text{H}_{21}\text{N}_2$ [$\text{M}+\text{H}$] $^+$ 265.1699; found 265.1694.



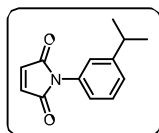
2-Phenyl-1H-pyrrolo[3,4-c]quinoline-1,3-dione (**6**)



To a solution of **3aa** (31.0 mg, 0.1 mmol) in toluene (1 mL) was added DDQ (47.5 mg, 0.2 mmol, 2 equiv) at room temperature. After being stirred for 2 h at 130 °C, the mixture was cooled to ambient temperature, and solvent was removed. Silica gel column chromatography of the crude mixture afforded the desired product **6** (0.021 g, 76% yield) and obtained characterization data were in alignment with the literature reported data.

^1H NMR (500 MHz, CDCl_3) δ 9.46 (s, 1H), 8.90 (dd, J = 8.3, 0.6 Hz, 1H), 8.30 (d, J = 8.6 Hz, 1H), 7.97 (ddd, J = 8.5, 7.0, 1.3 Hz, 1H), 7.86 – 7.79 (m, 1H), 7.59 – 7.52 (m, 2H), 7.47 (ddd, J = 16.2, 5.3, 1.2 Hz, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 167.3, 166.8, 152.3, 143.9, 135.2, 133.0, 131.2, 130.49, 130.41, 129.4, 128.6, 126.7, 125.2, 123.5, 121.6.

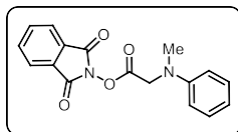
1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-phenylglycinate (**2k**)



The compound was prepared according to GP1 using 3-Isopropylaniline (0.5 g, 3.69 mmol, 1.0 equiv), and Furan-2,5-dione (0.72 g, 7.38 mmol, 2.0 equiv). Purification by column chromatography (20% ethyl acetate in hexane) gave **2k** as a yellow solid (0.44 g, 55%).

^1H NMR (500 MHz, CDCl_3) δ 7.39 (t, J = 7.8 Hz, 1H), 7.25 (d, J = 7.8 Hz, 1H), 7.17 (t, J = 1.9 Hz, 1H), 7.13 (ddd, J = 7.9, 2.0, 1.1 Hz, 1H), 6.84 (s, 2H), 2.95 (hept, J = 6.9 Hz, 1H), 1.27 (d, J = 6.9 Hz, 6H). ^{13}C NMR (126 MHz, CDCl_3) δ 169.7, 150.2, 134.2, 131.1, 129.1, 126.3, 124.5, 123.7, 34.0, 23.9. HRMS-ESI (m/z): calcd for $\text{C}_{13}\text{H}_{14}\text{NO}_2$ [$\text{M}+\text{H}$] $^+$ 216.1019; found 216.1022.

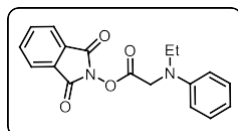
1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-phenylglycinate (1a)



The compound was prepared according to GP2 using *N*-Methyl-*N*-phenylglycine (3.304 g, 20.0 mmol, 1.0 equiv), 2-Hydroxyisindoline-1,3-dione (3.262 g, 20.0 mmol, 1.0 equiv) and DCC (4.126 g, 20.0 mmol, 1.0 equiv) and DMAP (0.244 g, 0.2 mmol, 0.1 equiv). Purification by column chromatography (20% ethyl acetate in hexane) gave **1a** as a white solid (3.4 g, 55%) and obtained characterization data were in alignment with the literature reported data.²

^1H NMR (500 MHz, CDCl_3) δ 7.86 (dd, J = 5.5, 3.1 Hz, 2H), 7.76 (dd, J = 5.5, 3.1 Hz, 2H), 7.33 – 7.27 (m, 2H), 6.82 (dd, J = 12.2, 4.9 Hz, 3H), 4.48 (s, 2H), 3.13 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 167.1, 161.8, 148.2, 134.9, 129.4, 128.8, 124.0, 118.4, 112.9, 52.2, 39.4.

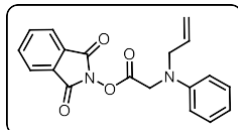
1,3-Dioxoisindolin-2-yl *N*-ethyl-*N*-phenylglycinate (1b)



The compound was prepared according to GP2 using *N*-Ethyl-*N*-phenylglycine (1.238 g, 6.0 mmol, 1.0 equiv), 2-Hydroxyisindoline-1,3-dione (0.978 g, 6.0 mmol, 1.0 equiv) and DCC (0.073 g, 6.0 mmol, 1.0 equiv) and DMAP (0.244 g, 0.2 mmol, 0.1 equiv). Purification by column chromatography (20% ethyl acetate in hexane) gave **1b** as a white solid (0.6 g, 31%).

^1H NMR (500 MHz, CDCl_3) δ 7.88 (dd, J = 5.5, 3.1 Hz, 2H), 7.78 (dd, J = 5.5, 3.1 Hz, 2H), 7.32 – 7.24 (m, 2H), 6.81 – 6.74 (m, 3H), 4.45 (s, 2H), 3.54 (q, J = 7.1 Hz, 2H), 1.27 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 167.7, 161.8, 147.1, 134.8, 129.4, 128.8, 124.0, 117.9, 112.6, 50.0, 46.1, 12.5. HRMS-ESI (m/z): calcd for $\text{C}_{18}\text{H}_{17}\text{N}_2\text{O}_4$ [$\text{M}+\text{H}$] $^+$ 325.1188; found 325.1184.

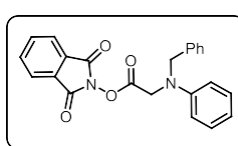
1,3-Dioxoisindolin-2-yl *N*-allyl-*N*-phenylglycinate (1c)



The compound was prepared according to GP2 using *N*-Allyl-*N*-phenylglycine (1.147 g, 6.0 mmol, 1.0 equiv), 2-Hydroxyisindoline-1,3-dione (0.978 g, 6.0 mmol, 1.0 equiv) and DCC (0.073 g, 6.0 mmol, 1.0 equiv) and DMAP (0.244 g, 0.2 mmol, 0.1 equiv). Purification by column chromatography (20% ethyl acetate in hexane) gave **2c** as a white solid (0.65 g, 32%).

^1H NMR (500 MHz, CDCl_3) δ 7.90 (dd, J = 5.5, 3.1 Hz, 2H), 7.81 (dd, J = 5.5, 3.1 Hz, 2H), 7.33 – 7.28 (m, 2H), 6.87 – 6.77 (m, 3H), 5.95 (m, 1H), 5.30 (m, 2H), 4.47 (s, 2H), 4.10 (dd, J = 3.6, 1.5 Hz, 2H). ^{13}C NMR (126 MHz, CDCl_3) δ 167.5, 161.7, 147.7, 134.8, 133.2, 129.3, 128.8, 124.0, 118.4, 117.3, 113.1, 54.1, 49.7. HRMS-ESI (m/z): calcd for $\text{C}_{19}\text{H}_{17}\text{N}_2\text{O}_4$ [$\text{M}+\text{H}$] $^+$ 337.1183; found 337.1177.

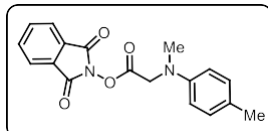
1,3-Dioxoisindolin-2-yl *N*-benzyl-*N*-phenylglycinate (1d)



The compound was prepared according to GP2 using *N*-Benzyl-*N*-phenylglycine (1.447 g, 6.0 mmol, 1.0 equiv), 2-Hydroxyisindoline-1,3-dione (0.978 g, 6.0 mmol, 1.0 equiv) and DCC (0.073 g, 6.0 mmol, 1.0 equiv) and DMAP (0.244 g, 0.2 mmol, 0.1 equiv). Purification by column chromatography (20% ethyl acetate in hexane) gave **1d** as a white solid (1.1 g, 47%).

^1H NMR (500 MHz, CDCl_3) δ 7.89 (dd, J = 5.2, 3.1 Hz, 2H), 7.79 (dd, J = 5.2, 3.1 Hz, 2H), 7.37 (dd, J = 13.5, 6.4 Hz, 3H), 7.33 – 7.24 (m, 4H), 6.85 (d, J = 7.3 Hz, 3H), 4.70 (s, 2H), 4.48 (s, 2H). ^{13}C NMR (126 MHz, CDCl_3) δ 167.4, 161.7, 148.0, 137.7, 134.8, 129.4, 128.8, 127.4, 127.0, 124.0, 118.7, 113.3, 55.5, 49.9. HRMS-ESI (m/z): calcd for $\text{C}_{23}\text{H}_{19}\text{N}_2\text{O}_4$ [$\text{M}+\text{H}$] $^+$ 387.1339; found 387.1350.

1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-(*p*-tolyl)glycinate (1e)

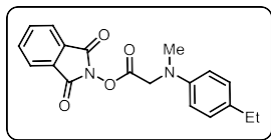


The compound was prepared according to GP2 using *N*-Methyl-*N*-(*p*-tolyl)glycine (1.075 g, 6.0 mmol, 1.0 equiv), 2-Hydroxyisindoline-1,3-dione (0.978 g, 6.0 mmol, 1.0 equiv) and DCC (0.073 g, 6.0 mmol, 1.0

equiv) and DMAP (0.244 g, 0.2 mmol, 0.1 equiv). Purification by column chromatography (20% ethyl acetate in hexane) gave **1e** as a white solid (0.72 g, 37%).

¹H NMR (500 MHz, CDCl₃) δ 7.87 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.78 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.10 (d, *J* = 8.5 Hz, 2H), 6.73 (d, *J* = 8.6 Hz, 2H), 4.45 (s, 2H), 3.10 (s, 3H), 2.26 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 167.1, 161.7, 146.0, 134.8, 129.9, 128.8, 127.6, 124.0, 113.1, 52.4, 39.5, 20.3. HRMS-ESI (*m/z*): calcd for C₁₈H₁₇N₂O₄ [M+H]⁺ 325.1188; found 325.1184.

1,3-Dioxoisindolin-2-yl *N*-(4-ethylphenyl)-*N*-methylglycinate (**1f**)

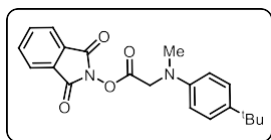


The compound was prepared according to GP2 using *N*-(4-ethylphenyl)-*N*-methylglycine (1.159 g, 6.0 mmol, 1.0 equiv), 2-Hydroxyisindoline-1,3-dione (0.978 g, 6.0 mmol, 1.0 equiv) and DCC (0.073 g, 6.0 mmol, 1.0 equiv) and DMAP (0.244 g, 0.2 mmol, 0.1 equiv). Purification by column chromatography (20% ethyl acetate in hexane) gave **1f** as a yellow solid (0.66 g, 37%).

¹H NMR (500 MHz, CDCl₃) δ 7.87 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.78 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.13 (d, *J* = 8.6 Hz, 2H), 6.76 (d, *J* = 8.7 Hz, 2H), 4.46 (s, 2H), 3.11 (s, 3H), 2.57 (q, *J* = 7.6 Hz, 2H), 1.20 (t, *J* = 7.6 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 167.1, 161.8, 146.2, 134.8, 134.1, 128.8, 128.7, 124.0, 113.1, 52.3, 39.4, 27.8, 15.7. HRMS-ESI (*m/z*): calcd for C₁₉H₁₉N₂O₄ [M+H]⁺ 339.1339; found 339.1358.

1,3-Dioxoisindolin-2-yl *N*-(4-(tert-butyl)phenyl)-*N*-methylglycinate (**1g**)

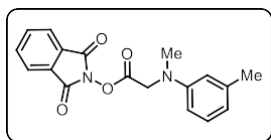


The compound was prepared according to GP2 using *N*-(4-(tert-butyl)phenyl)-*N*-methylglycine (1.327 g, 6.0 mmol, 1.0 equiv), 2-Hydroxyisindoline-1,3-dione (0.978 g, 6.0 mmol, 1.0 equiv) and DCC (0.073 g, 6.0 mmol, 1.0 equiv) and DMAP (0.244 g, 0.2 mmol, 0.1 equiv).

Purification by column chromatography (20% ethyl acetate in hexane) gave **1g** as a yellow solid (0.96 g, 44%).

¹H NMR (500 MHz, CDCl₃) δ 7.88 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.78 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.32 (d, *J* = 8.9 Hz, 2H), 6.76 (d, *J* = 8.9 Hz, 2H), 4.46 (s, 2H), 3.12 (s, 3H), 1.29 (s, 9H). ¹³C NMR (126 MHz, CDCl₃) δ 167.1, 161.8, 145.9, 140.9, 134.8, 128.8, 126.1, 124.0, 112.6, 52.2, 39.3, 33.8, 31.5. HRMS-ESI (*m/z*): calcd for C₂₁H₂₃N₂O₄ [M+H]⁺ 367.1652; found 367.1664.

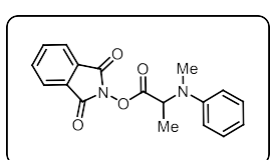
1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-(*m*-tolyl)glycinate (**1h**)



The compound was prepared according to GP2 using *N*-Methyl-*N*-(*m*-tolyl)glycine (1.075 g, 6.0 mmol, 1.0 equiv), 2-Hydroxyisindoline-1,3-dione (0.978 g, 6.0 mmol, 1.0 equiv) and DCC (0.073 g, 6.0 mmol, 1.0 equiv) and DMAP (0.244 g, 0.2 mmol, 0.1 equiv). Purification by column chromatography (20% ethyl acetate in hexane) gave **1h** as a white solid (0.68 g, 35%).

¹H NMR (500 MHz, CDCl₃) δ 7.87 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.77 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.21 – 7.15 (m, 1H), 6.67 – 6.60 (m, 3H), 4.47 (s, 2H), 3.13 (s, 3H), 2.36 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 167.1, 161.7, 148.2, 139.1, 134.8, 129.2, 128.8, 124.0, 119.3, 113.7, 110.1, 52.2, 39.4, 21.8. HRMS-ESI (*m/z*): calcd for C₁₈H₁₇N₂O₄ [M+H]⁺ 325.1183; found 325.1192.

1,3-dioxoisindolin-2-yl *N*-methyl-*N*-phenylalaninate (**1i**)

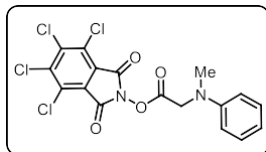


The compound was prepared according to GP2 using *N*-methyl-*N*-phenylalanine (1.075 g, 6.0 mmol, 1.0 equiv), 2-Hydroxyisindoline-1,3-dione (1.805 g, 6.0 mmol, 1.0 equiv) and DCC (0.073 g, 6.0 mmol, 1.0 equiv) and DMAP (0.244 g, 0.2 mmol, 0.1 equiv). Purification by column chromatography (20% ethyl acetate in hexane) gave **1i** as a yellow solid

(1.2 g, 62%).

¹H NMR (500 MHz, CDCl₃) δ 7.86 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.77 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.30 (dd, *J* = 8.7, 7.3 Hz, 2H), 6.93 (d, *J* = 8.2 Hz, 2H), 6.83 (t, *J* = 7.3 Hz, 1H), 4.95 (q, *J* = 7.1 Hz, 1H), 2.99 (s, 3H), 1.66 (d, *J* = 7.1 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 169.4, 161.8, 149.2, 134.8, 129.3, 128.9, 124.08, 124.05, 118.8, 114.3, 56.0, 33.1, 15.3. HRMS-ESI (*m/z*): calcd for C₁₈H₁₇N₂O₄ [M+H]⁺ 325.1188; found 325.1197.

4,5,6,7-Tetrachloro-1,3-dioxoisindolin-2-yl *N*-methyl-*N*-phenylglycinate (**1j**)

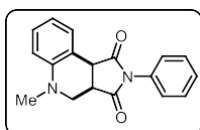


The compound was prepared according to GP2 using *N*-Methyl-*N*-phenylglycine (0.991 g, 6.0 mmol, 1.0 equiv), 4,5,6,7-Tetrachloro-2-hydroxyisindoline-1,3-dione (1.805 g, 6.0 mmol, 1.0 equiv) and DCC (0.073 g, 6.0 mmol, 1.0 equiv) and DMAP (0.244 g, 0.2 mmol, 0.1 equiv).

Purification by column chromatography (20% ethyl acetate in hexane) gave **1j** as an orange solid (1.65 g, 62%).

¹H NMR (500 MHz, CDCl₃) δ 7.29 (dd, *J* = 8.6, 7.4 Hz, 2H), 6.82 (t, *J* = 7.3 Hz, 1H), 6.78 (d, *J* = 8.1 Hz, 2H), 4.48 (s, 2H), 3.12 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 166.7, 157.4, 148.0, 141.2, 130.6, 129.5, 124.7, 118.6, 112.9, 52.2, 39.4. HRMS-ESI (*m/z*): calcd for C₁₇H₁₁Cl₄N₂O₄ [M+H]⁺ 446.9467; found 446.9469.

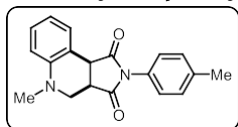
5-Methyl-2-phenyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-*c*]quinoline-1,3(2H)-dione (**3aa**)



The compound was prepared according to GP-1 using 1-Phenyl-1H-pyrrole-2,5-dione (0.043 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-phenylglycinate (0.232 g, 0.75 mmol) and DIPEA (130.6 μL, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in hexane) gave **3aa** as a white solid (0.053 g, 72%).

¹H NMR (500 MHz, CDCl₃) δ 7.53 (d, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 2H), 7.36 (dd, *J* = 8.3, 6.3 Hz, 1H), 7.25 (dd, *J* = 15.5, 7.3 Hz, 3H), 6.91 (t, *J* = 7.2 Hz, 1H), 6.75 (d, *J* = 8.3 Hz, 1H), 4.17 (d, *J* = 9.6 Hz, 1H), 3.62 (dd, *J* = 11.4, 2.8 Hz, 1H), 3.54 (ddd, *J* = 9.7, 4.1, 2.8 Hz, 1H), 3.13 (dd, *J* = 11.5, 4.3 Hz, 1H), 2.84 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 177.8, 175.9, 148.6, 132.1, 130.4, 129.1, 128.8, 128.6, 126.4, 119.8, 118.6, 112.6, 50.7, 43.7, 42.2, 39.5.

5-Methyl-2-(*p*-tolyl)-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-*c*]quinoline-1,3(2H)-dione (**3ab**)

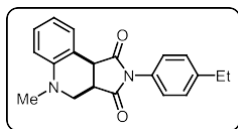


The compound was prepared according to GP-1 using 1-(*p*-tolyl)-1H-pyrrole-2,5-dione (0.047 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-phenylglycinate (0.232 g, 0.75 mmol) and DIPEA (130.6 μL, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in hexane) gave

3ab as a white solid (0.057 g, 74%).

¹H NMR (500 MHz, CDCl₃) δ 7.53 (d, *J* = 7.3 Hz, 1H), 7.23 (d, *J* = 8.2 Hz, 3H), 7.14 (d, *J* = 8.4 Hz, 2H), 6.91 (td, *J* = 7.5, 1.0 Hz, 1H), 6.74 (d, *J* = 8.2 Hz, 1H), 4.15 (d, *J* = 9.6 Hz, 1H), 3.61 (dd, *J* = 11.5, 2.8 Hz, 1H), 3.53 (ddd, *J* = 9.6, 4.4, 2.8 Hz, 1H), 3.12 (dd, *J* = 11.5, 4.4 Hz, 1H), 2.84 (s, 3H), 2.36 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 177.8, 175.9, 148.5, 138.5, 130.3, 129.6, 129.3, 128.6, 126.1, 119.6, 118.6, 112.5, 50.6, 43.5, 42.1, 39.4, 21.2.

2-(4-Ethylphenyl)-5-methyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-*c*]quinoline-1,3(2H)-dione (**3ac**)



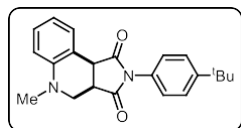
The compound was prepared according to GP-1 using 1-(4-Ethylphenyl)-1H-pyrrole-2,5-dione (0.050 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-phenylglycinate (0.232 g, 0.75 mmol) and DIPEA (130.6 μL, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in

hexane) gave **3ac** as a white solid (0.070 g, 87%).

¹H NMR (500 MHz, CDCl₃) δ 7.53 (d, *J* = 7.3 Hz, 1H), 7.26 – 7.22 (m, 3H), 7.19 – 7.15 (m, 2H), 6.91 (td, *J* = 7.5, 0.9 Hz, 1H), 6.74 (d, *J* = 8.1 Hz, 1H), 4.15 (d, *J* = 9.6 Hz, 1H), 3.61 (dd, *J* = 11.5, 2.8 Hz, 1H), 3.53 (ddd, *J* = 9.5, 4.4, 2.8 Hz, 1H), 3.12 (dd, *J* = 11.5, 4.4 Hz, 1H), 2.84 (s, 3H), 2.65 (q, *J* = 7.6 Hz, 2H), 1.22 (t, *J* = 7.6 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 177.8, 175.9, 148.5, 144.7, 130.3, 129.4, 128.6, 128.5, 126.2, 119.6, 118.6, 112.5, 50.6, 43.5, 42.1, 39.4, 28.5, 15.4.

2-(4-(Tert-butyl)phenyl)-5-methyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-*c*]quinoline-1,3(2H)-dione (**3ad**)

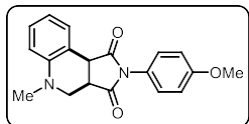
The compound was prepared according to GP-1 using 1-(4-(Tert-butyl)phenyl)-1H-pyrrole-2,5-dione (0.057 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-phenylglycinate (0.232 g, 0.75



mmol) and DIPEA (130.6 μ L, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in hexane) gave **3ad** as a white solid (0.082 g, 94%).

^1H NMR (500 MHz, CDCl_3) δ 7.54 (d, J = 7.4 Hz, 1H), 7.44 (d, J = 8.6 Hz, 2H), 7.26 – 7.21 (m, 1H), 7.19 (d, J = 8.6 Hz, 2H), 6.91 (td, J = 7.5, 0.7 Hz, 1H), 6.74 (d, J = 8.2 Hz, 1H), 4.15 (d, J = 9.6 Hz, 1H), 3.61 (dd, J = 11.5, 2.8 Hz, 1H), 3.54 (ddd, J = 9.5, 4.3, 2.8 Hz, 1H), 3.12 (dd, J = 11.5, 4.4 Hz, 1H), 2.84 (s, 3H), 1.31 (s, 9H). ^{13}C NMR (126 MHz, CDCl_3) δ 177.9, 175.9, 151.5, 148.5, 130.3, 129.2, 128.6, 126.0, 125.7, 119.6, 118.6, 112.5, 50.6, 43.5, 42.1, 39.4, 34.7, 31.2. HRMS-ESI (m/z): calcd for $\text{C}_{22}\text{H}_{24}\text{N}_2\text{O}_2\text{Na}$ [$\text{M}+\text{Na}$] $^+$ 371.1730; found 371.1724.

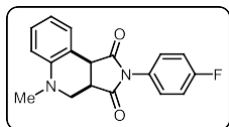
2-(4-Methoxyphenyl)-5-methyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (**3ae**)



The compound was prepared according to GP-1 using 1-(4-Methoxyphenyl)-1H-pyrrole-2,5-dione (0.051 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-phenylglycinate (0.232 g, 0.75 mmol) and DIPEA (130.6 μ L, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in hexane) gave **3ae** as a white solid (0.063 g, 78%).

^1H NMR (500 MHz, CDCl_3) δ 7.53 (d, J = 7.4 Hz, 1H), 7.24 (t, J = 8.0 Hz, 1H), 7.18 (d, J = 8.9 Hz, 2H), 6.96 – 6.90 (m, 3H), 6.74 (d, J = 8.2 Hz, 1H), 4.14 (d, J = 9.6 Hz, 1H), 3.80 (s, 3H), 3.60 (dd, J = 11.5, 2.5 Hz, 1H), 3.55 – 3.49 (m, 1H), 3.12 (dd, J = 11.5, 4.4 Hz, 1H), 2.84 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 178.0, 176.1, 159.5, 148.6, 130.4, 128.7, 127.7, 124.7, 119.7, 118.7, 114.4, 112.6, 55.5, 50.8, 43.6, 42.1, 39.5.

2-(4-Fluorophenyl)-5-methyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (**3af**)

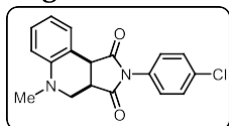


The compound was prepared according to GP-1 using 1-(4-Fluorophenyl)-1H-pyrrole-2,5-dione (0.048 g, 0.25 mmol), 1,3-dioxoisindolin-2-yl *N*-methyl-*N*-phenylglycinate (0.232 g, 0.75 mmol) and DIPEA (130.6 μ L, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in

hexane) gave **3af** as a white solid (0.033 g, 43%).

^1H NMR (500 MHz, CDCl_3) δ 7.52 (d, J = 7.3 Hz, 1H), 7.28 – 7.24 (m, 3H), 7.14 – 7.08 (m, 2H), 6.91 (td, J = 7.5, 1.0 Hz, 1H), 6.75 (d, J = 8.1 Hz, 1H), 4.16 (d, J = 9.6 Hz, 1H), 3.61 (dd, J = 11.5, 2.6 Hz, 1H), 3.54 (ddd, J = 9.6, 4.3, 2.6 Hz, 1H), 3.12 (dd, J = 11.5, 4.4 Hz, 1H), 2.84 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 177.8, 175.8, 162.2 (d, J = 248.4 Hz), 148.6, 130.4, 128.9, 128.3 (d, J = 8.7 Hz), 127.9 (d, J = 3.3 Hz), 119.8, 118.5, 116.1 (d, J = 22.9 Hz), 112.7, 50.7, 43.7, 42.2, 39.5. ^{19}F NMR (471 MHz, CDCl_3) δ -112.38.

2-(4-Chlorophenyl)-5-methyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (**3ag**)



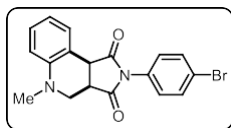
The compound was prepared according to GP-1 using 1-(4-Chlorophenyl)-1H-pyrrole-2,5-dione (0.052 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-phenylglycinate (0.232 g, 0.75 mmol) and DIPEA (130.6 μ L, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in

hexane) gave **3ag** as a white solid (0.040 g, 49%).

^1H NMR (500 MHz, CDCl_3) δ 7.52 (d, J = 7.4 Hz, 1H), 7.42 – 7.37 (m, 2H), 7.26 – 7.23 (m, 3H), 6.92 (t, J = 7.4 Hz, 1H), 6.75 (d, J = 8.2 Hz, 1H), 4.16 (d, J = 9.6 Hz, 1H), 3.61 (dd, J = 11.5, 2.6 Hz, 1H), 3.54 (ddd, J = 9.6, 4.2, 2.7 Hz, 1H), 3.12 (dd, J = 11.5, 4.4 Hz, 1H), 2.84 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 177.6, 175.6, 148.6, 134.3, 130.5, 130.4, 129.3, 128.9, 127.7, 119.8, 118.4, 112.7, 50.7, 43.7, 42.2, 39.5.

2,5-Dimethyl-3a,4,5,9b-2-(4-bromophenyl)-5-methyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (**3ah**)

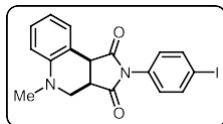
The compound was prepared according to GP-1 using 1-(4-Bromophenyl)-1H-pyrrole-2,5-dione (0.052 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-phenylglycinate (0.232 g, 0.75 mmol)



and DIPEA (130.6 μ L, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in hexane) gave **3ah** as a white solid (0.042g, 45%).

^1H NMR (500 MHz, CDCl_3) δ 7.57 – 7.53 (m, 2H), 7.51 (d, J = 7.3 Hz, 1H), 7.26 – 7.22 (m, 1H), 7.21 – 7.16 (m, 2H), 6.91 (td, J = 7.5, 1.0 Hz, 1H), 6.75 (d, J = 8.2 Hz, 1H), 4.16 (d, J = 9.6 Hz, 1H), 3.61 (dd, J = 11.5, 2.6 Hz, 1H), 3.53 (ddd, J = 9.6, 4.3, 2.6 Hz, 1H), 3.11 (dd, J = 11.5, 4.4 Hz, 1H), 2.83 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 177.5, 175.5, 148.6, 132.2, 131.0, 130.4, 128.9, 127.9, 122.4, 119.8, 118.4, 112.7, 50.7, 43.7, 42.2, 39.5.

2-(4-Iodophenyl)-5-methyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (3ai)

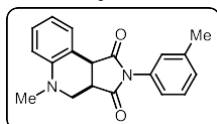


The compound was prepared according to GP-1 using 1-(4-Iodophenyl)-1H-pyrrole-2,5-dione (0.075 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-phenylglycinate (0.232 g, 0.75 mmol) and DIPEA (130.6 μ L, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in hexane) gave

3ai as a white solid (0.055 g, 53%).

^1H NMR (500 MHz, CDCl_3) δ 7.75 (d, J = 8.6 Hz, 2H), 7.51 (d, J = 7.4 Hz, 1H), 7.26 – 7.22 (m, 1H), 7.05 (d, J = 8.6 Hz, 2H), 6.91 (t, J = 7.2 Hz, 1H), 6.74 (d, J = 8.2 Hz, 1H), 4.16 (d, J = 9.6 Hz, 1H), 3.61 (dd, J = 11.5, 2.6 Hz, 1H), 3.53 (ddd, J = 9.6, 4.3, 2.6 Hz, 1H), 3.11 (dd, J = 11.5, 4.4 Hz, 1H), 2.83 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 177.5, 175.5, 148.6, 138.2, 131.7, 130.4, 128.9, 128.1, 119.9, 118.4, 112.7, 94.0, 50.7, 43.7, 42.2, 39.5. HRMS-ESI (m/z): calcd for $\text{C}_{18}\text{H}_{16}\text{IN}_2\text{O}_2$ [$\text{M}+\text{H}$] $^+$ 419.0251; found 419.0254.

5-Methyl-2-(*m*-tolyl)-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (3aj)

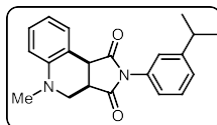


The compound was prepared according to GP-1 using 1-(*m*-tolyl)-1H-pyrrole-2,5-dione (0.047 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-phenylglycinate (0.232 g, 0.75 mmol) and DIPEA (130.6 μ L, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in hexane) gave

3aj as a white solid (0.062 g, 81%).

^1H NMR (500 MHz, CDCl_3) δ 7.53 (d, J = 7.4 Hz, 1H), 7.33 – 7.29 (m, 1H), 7.25 – 7.22 (m, 1H), 7.17 (d, J = 7.6 Hz, 1H), 7.05 (d, J = 5.8 Hz, 2H), 6.91 (t, J = 7.5 Hz, 1H), 6.75 (d, J = 8.2 Hz, 1H), 4.16 (d, J = 9.6 Hz, 1H), 3.61 (dd, J = 11.5, 2.7 Hz, 1H), 3.53 (ddd, J = 9.6, 4.4, 2.7 Hz, 1H), 3.12 (dd, J = 11.5, 4.4 Hz, 1H), 2.84 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 177.9, 176.0, 148.6, 139.2, 131.9, 130.4, 129.5, 128.9, 128.8, 127.1, 123.6, 119.7, 118.7, 112.6, 50.7, 43.7, 42.2, 39.5, 21.4. HRMS-ESI (m/z): calcd for $\text{C}_{19}\text{H}_{19}\text{N}_2\text{O}_2$ [$\text{M}+\text{H}$] $^+$ 307.1441; found 307.1446.

2-(3-Isopropylphenyl)-5-methyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (3ak)

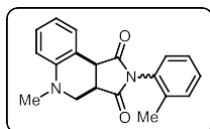


The compound was prepared according to GP-1 using 1-(3-Isopropylphenyl)-1H-pyrrole-2,5-dione (0.053 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-phenylglycinate (0.232 g, 0.75 mmol) and DIPEA (130.6 μ L, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in

hexane) gave **3ak** as a white solid (0.075 g, 90%).

^1H NMR (500 MHz, CDCl_3) δ 7.56 (d, J = 7.3 Hz, 1H), 7.36 (t, J = 7.8 Hz, 1H), 7.27 – 7.23 (m, 2H), 7.13 (t, J = 1.8 Hz, 1H), 7.09 (ddd, J = 7.9, 2.0, 1.1 Hz, 1H), 6.93 (td, J = 7.5, 1.0 Hz, 1H), 6.77 (d, J = 7.8 Hz, 1H), 4.18 (d, J = 9.6 Hz, 1H), 3.63 (dd, J = 11.5, 2.8 Hz, 1H), 3.56 (ddd, J = 9.6, 4.4, 2.8 Hz, 1H), 3.18 – 3.13 (m, 1H), 2.93 (dt, J = 13.8, 6.9 Hz, 1H), 2.87 (s, 3H), 1.25 (d, J = 6.9 Hz, 6H). ^{13}C NMR (126 MHz, CDCl_3) δ 177.8, 175.8, 149.9, 148.5, 131.8, 130.3, 128.8, 128.6, 126.6, 124.5, 123.7, 119.6, 118.6, 112.5, 50.7, 43.5, 42.1, 39.4, 34.0, 23.8. HRMS-ESI (m/z): calcd for $\text{C}_{21}\text{H}_{23}\text{N}_2\text{O}_2$ [$\text{M}+\text{H}$] $^+$ 335.1754; found 335.1762.

5-Methyl-2-(*o*-tolyl)-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (3al)

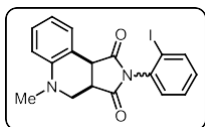


The compound was prepared according to GP-1 using 1-(*o*-tolyl)-1H-pyrrole-2,5-dione (0.047 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-phenylglycinate (0.232 g, 0.75 mmol) and DIPEA (130.6 μ L, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in hexane) gave

3al (nonseparable mixture of two diastereomers) as a white solid (dr = 2.1:1, 0.057 g, 74%).

¹H NMR (500 MHz, CDCl₃) δ 7.51 (t, *J* = 8.5 Hz, 1H), 7.30 (ddd, *J* = 6.5, 4.9, 2.6 Hz, 2H), 7.26 – 7.19 (m, 2H), 7.15 – 7.10 (m, 1H), 6.91 (dt, *J* = 7.4, 4.1 Hz, 1H), 6.76 (t, *J* = 8.5 Hz, 1H), 4.19 (dd, *J* = 14.5, 9.3 Hz, 1H), 3.65 – 3.54 (m, 2H), 3.12 (ddd, *J* = 15.6, 11.3, 4.1 Hz, 1H), 2.86 (s, 1H), 2.85 (s, 2H), 2.20 (s, 1H), 1.84 (s, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 177.9, 177.6, 175.8, 175.7, 148.6, 148.5, 135.9, 135.3, 131.1, 131.0, 130.37, 130.35, 129.5, 129.4, 128.7, 128.1, 127.8, 126.85, 126.80, 119.8, 119.7, 118.9, 118.6, 112.5, 112.3, 51.1, 50.8, 44.3, 43.7, 42.8, 42.3, 39.5, 39.2, 17.8, 17.0.

2-(2-Iodophenyl)-5-methyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (3am)

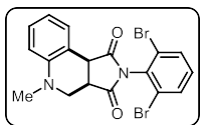


The compound was prepared according to GP-1 using 1-(2-Iodophenyl)-1H-pyrrole-2,5-dione (0.075 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-phenylglycinate (0.232 g, 0.75 mmol) and DIPEA (130.6 μL, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in hexane) gave

3am (nonseparable mixture of two diastereomers) as a white solid (dr = 1:1, 0.057 g, 55%).

¹H NMR (500 MHz, CDCl₃) δ 7.95 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.89 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.56 (t, *J* = 7.3 Hz, 2H), 7.47 (td, *J* = 7.7, 1.3 Hz, 1H), 7.41 (td, *J* = 7.7, 1.3 Hz, 1H), 7.28 – 7.21 (m, 3H), 7.17 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.15 – 7.12 (m, 1H), 7.12 – 7.08 (m, 1H), 6.92 (m, *J* = 8.4, 7.5, 1.0 Hz, 2H), 6.79 (d, *J* = 8.2 Hz, 1H), 6.73 (d, *J* = 8.2 Hz, 1H), 4.28 (d, *J* = 9.9 Hz, 1H), 4.21 (d, *J* = 9.4 Hz, 1H), 3.70 (dd, *J* = 11.5, 3.1 Hz, 1H), 3.68 – 3.62 (m, 2H), 3.59 (ddd, *J* = 9.3, 4.1, 3.2 Hz, 1H), 3.25 (dd, *J* = 11.5, 4.2 Hz, 1H), 3.16 (dd, *J* = 11.6, 4.6 Hz, 1H), 2.90 (s, 3H), 2.88 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 177.0, 176.9, 175.05, 175.03, 148.7, 148.6, 140.3, 139.8, 135.6, 135.4, 131.1, 130.9, 130.49, 130.45, 129.7, 129.5, 129.4, 129.3, 128.87, 128.86, 119.8, 119.4, 118.5, 117.8, 112.7, 112.3, 97.7, 97.3, 50.6, 50.2, 44.19, 44.17, 42.7, 42.6, 39.6, 39.3. HRMS-ESI (*m/z*): calcd for C₁₈H₁₆N₂O₂ [M+H]⁺ 419.0256; found 419.0248.

2-(2,6-Dibromophenyl)-5-methyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (3an)

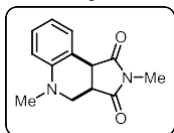


The compound was prepared according to GP-1 using 1-(2,6-Dibromophenyl)-1H-pyrrole-2,5-dione (0.083 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-phenylglycinate (0.232 g, 0.75 mmol) and DIPEA (130.6 μL, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in hexane) gave

3an as a white solid (0.053 g, 47%).

¹H NMR (500 MHz, CDCl₃) δ 7.52 (d, *J* = 7.3 Hz, 1H), 7.43 – 7.38 (m, 2H), 7.27 (d, *J* = 1.5 Hz, 1H), 7.24 (dd, *J* = 3.4, 1.7 Hz, 1H), 6.92 (td, *J* = 7.5, 1.0 Hz, 1H), 6.76 (d, *J* = 8.1 Hz, 1H), 4.17 (d, *J* = 9.6 Hz, 1H), 3.62 (dd, *J* = 11.5, 2.6 Hz, 1H), 3.54 (ddd, *J* = 9.6, 4.3, 2.6 Hz, 1H), 3.12 (dd, *J* = 11.5, 4.4 Hz, 1H), 2.84 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 177.6, 175.6, 148.6, 134.3, 130.5, 130.4, 129.3, 128.9, 127.7, 119.9, 118.4, 112.7, 50.7, 43.7, 42.2, 39.5. HRMS-ESI (*m/z*): calcd for C₁₈H₁₅Br₂N₂O₂ [M+H]⁺ 448.9495; found 448.9495.

Tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (3ao)

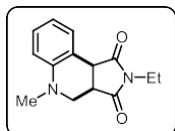


The compound was prepared according to GP-1 using 1-Methyl-1H-pyrrole-2,5-dione (0.277 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-phenylglycinate (0.232 g, 0.75 mmol) and DIPEA (130.6 μL, 0.75 mmol). Purification by column chromatography (25% ethyl acetate in hexane) gave **3ao**

as a white solid (0.038 g, 65%).

¹H NMR (500 MHz, CDCl₃) δ 7.47 (d, *J* = 7.4 Hz, 1H), 7.24 – 7.18 (m, 1H), 6.89 (td, *J* = 7.5, 0.9 Hz, 1H), 6.69 (d, *J* = 8.2 Hz, 1H), 3.99 (d, *J* = 9.4 Hz, 1H), 3.53 (dd, *J* = 11.5, 2.4 Hz, 1H), 3.36 (ddd, *J* = 9.4, 4.4, 2.4 Hz, 1H), 3.03 (dd, *J* = 11.5, 4.5 Hz, 1H), 2.98 (s, 3H), 2.79 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 178.8, 176.9, 148.4, 130.2, 128.6, 119.6, 118.8, 112.5, 50.5, 43.6, 42.1, 39.4, 25.4.

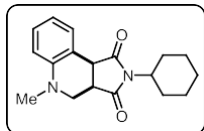
2-Ethyl-5-methyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (3ap)



The compound was prepared according to GP-1 using 1-Ethyl-1*H*-pyrrole-2,5-dione (0.031 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-phenylglycinate (0.232 g, 0.75 mmol) and DIPEA (130.6 μ L, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in hexane) gave **3ap** as a white solid (0.038 g, 62%).

¹H NMR (500 MHz, CDCl₃) δ 7.47 (d, *J* = 7.4 Hz, 1H), 7.24 – 7.18 (m, 1H), 6.89 (td, *J* = 7.5, 1.0 Hz, 1H), 6.70 (d, *J* = 7.7 Hz, 1H), 3.97 (d, *J* = 9.4 Hz, 1H), 3.58 – 3.51 (m, 2H), 3.51 – 3.48 (m, 1H), 3.34 (ddd, *J* = 9.4, 4.5, 2.7 Hz, 1H), 3.03 (dd, *J* = 11.5, 4.6 Hz, 1H), 2.79 (s, 3H), 1.13 (t, *J* = 7.2 Hz, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 178.6, 176.6, 148.5, 130.3, 128.6, 119.6, 118.9, 112.5, 50.7, 43.5, 42.0, 39.5, 34.3, 13.0.

2-Cyclohexyl-5-methyl-3a,4,5,9b-tetrahydro-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**3aq**)

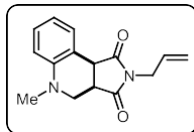


The compound was prepared according to GP-1 using 1-Cyclohexyl-1*H*-pyrrole-2,5-dione (0.044 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-phenylglycinate (0.232 g, 0.75 mmol) and DIPEA (130.6 μ L, 0.75 mmol). Purification by column chromatography (15% ethyl acetate in hexane) gave

3aq as a orange oil (0.063 g, 84%).

¹H NMR (500 MHz, CDCl₃) δ 7.46 (d, *J* = 7.4 Hz, 1H), 7.22 – 7.16 (m, 1H), 6.88 (td, *J* = 7.5, 0.8 Hz, 1H), 6.69 (d, *J* = 8.1 Hz, 1H), 3.94 (ddd, *J* = 12.3, 8.1, 3.8 Hz, 1H), 3.89 (d, *J* = 9.5 Hz, 1H), 3.45 (dd, *J* = 11.4, 2.9 Hz, 1H), 3.27 (ddd, *J* = 9.4, 4.5, 2.9 Hz, 1H), 3.02 (dd, *J* = 11.4, 4.6 Hz, 1H), 2.78 (s, 3H), 2.09 (m, 2H), 1.82 – 1.73 (m, 2H), 1.65 – 1.48 (m, 3H), 1.25 (m, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 178.7, 176.8, 148.4, 130.2, 128.4, 119.5, 119.0, 112.4, 52.1, 50.8, 43.0, 41.7, 39.4, 28.8, 28.7, 25.8, 25.7, 25.0.

2-Allyl-5-methyl-3a,4,5,9b-tetrahydro-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**3ar**)

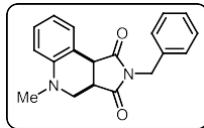


The compound was prepared according to GP-1 using 1-Allyl-1*H*-pyrrole-2,5-dione (0.034 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-phenylglycinate (0.232 g, 0.75 mmol) and DIPEA (130.6 μ L, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in hexane) gave

3ar as a pale-yellow oil (0.054 g, 85%).

¹H NMR (500 MHz, CDCl₃) δ 7.47 (d, *J* = 7.3 Hz, 1H), 7.24 – 7.17 (m, 1H), 6.90 (td, *J* = 7.5, 1.0 Hz, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 5.74 (ddt, *J* = 17.0, 10.7, 5.4 Hz, 1H), 5.12 – 5.09 (m, 1H), 5.10 – 5.06 (m, 1H), 4.10 (ddt, *J* = 7.0, 5.4, 1.5 Hz, 2H), 4.02 (d, *J* = 9.4 Hz, 1H), 3.52 (dd, *J* = 11.5, 2.5 Hz, 1H), 3.39 (ddd, *J* = 9.4, 4.5, 2.6 Hz, 1H), 3.04 (dd, *J* = 11.5, 4.5 Hz, 1H), 2.80 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 178.4, 176.4, 148.6, 130.4, 130.3, 128.7, 119.8, 118.9, 117.6, 112.6, 50.8, 43.7, 42.2, 41.3, 39.4.

2-Benzyl-5-methyl-3a,4,5,9b-tetrahydro-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**3as**)

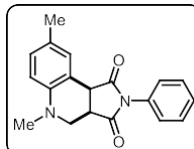


The compound was prepared according to GP-1 using 1-Benzyl-1*H*-pyrrole-2,5-dione (0.047 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-phenylglycinate (0.232 g, 0.75 mmol) and DIPEA (130.6 μ L, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in hexane) gave

3as as a white solid (0.061 g, 79%).

¹H NMR (500 MHz, CDCl₃) δ 7.47 (d, *J* = 7.2 Hz, 1H), 7.32 – 7.21 (m, 6H), 6.90 (td, *J* = 7.5, 1.1 Hz, 1H), 6.71 (d, *J* = 8.2 Hz, 1H), 4.65 (dd, *J* = 32.4, 14.3 Hz, 2H), 4.00 (d, *J* = 9.4 Hz, 1H), 3.50 (dd, *J* = 11.5, 2.7 Hz, 1H), 3.37 (ddd, *J* = 9.4, 4.5, 2.7 Hz, 1H), 3.05 (dd, *J* = 11.5, 4.5 Hz, 1H), 2.80 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 178.3, 176.4, 148.4, 135.5, 130.2, 128.62, 128.61, 128.3, 127.8, 119.7, 118.8, 112.4, 50.7, 43.6, 42.8, 42.0, 39.3.

5,8-Dimethyl-2-phenyl-3a,4,5,9b-tetrahydro-1*H*-pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**3ba**)

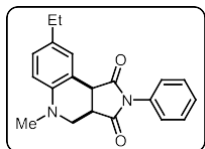


The compound was prepared according to GP-1 using 1-Phenyl-1*H*-pyrrole-2,5-dione (0.043 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-(*p*-tolyl)glycinate (0.243 g, 0.75 mmol) and DIPEA (130.6 μ L, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in hexane) gave

3ba as a white solid (0.050 g, 65%).

¹H NMR (500 MHz, CDCl₃) δ 7.43 (dd, *J* = 10.8, 4.5 Hz, 2H), 7.36 (dq, *J* = 6.5, 1.2 Hz, 2H), 7.28 (t, *J* = 1.7 Hz, 2H), 7.04 (dd, *J* = 8.1, 1.7 Hz, 1H), 6.65 (d, *J* = 8.3 Hz, 1H), 4.12 (d, *J* = 9.6 Hz, 1H), 3.59 (dd, *J* = 11.4, 2.7 Hz, 1H), 3.52 (ddd, *J* = 9.6, 4.3, 2.7 Hz, 1H), 3.06 (dd, *J* = 11.4, 4.4 Hz, 1H), 2.81 (s, 3H), 2.30 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 177.9, 176.0, 146.5, 132.1, 130.9, 129.3, 129.15, 129.13, 128.6, 126.5, 118.6, 112.6, 51.0, 43.7, 42.3, 39.7, 20.5.

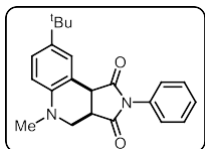
8-Ethyl-5-methyl-2-phenyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (3ca)



The compound was prepared according to GP-1 using 1-Phenyl-1H-pyrrole-2,5-dione (0.043 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-(4-ethylphenyl)-*N*-methylglycinate (0.254 g, 0.75 mmol) and DIPEA (130.6 μL, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in hexane) gave **3ca** as a white solid (0.040 g, 60%).

¹H NMR (500 MHz, CDCl₃) δ 7.53 (d, *J* = 7.3 Hz, 1H), 7.25 (dd, *J* = 6.9, 2.9 Hz, 3H), 7.20 – 7.14 (m, 2H), 6.91 (td, *J* = 7.5, 1.0 Hz, 1H), 6.75 (d, *J* = 7.8 Hz, 1H), 4.15 (d, *J* = 9.6 Hz, 1H), 3.61 (dd, *J* = 11.5, 2.8 Hz, 1H), 3.53 (ddd, *J* = 9.6, 4.4, 2.8 Hz, 1H), 3.12 (dd, *J* = 11.5, 4.4 Hz, 1H), 2.84 (s, 3H), 2.66 (q, *J* = 7.6 Hz, 2H), 1.22 (t, *J* = 7.6 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 177.9, 175.9, 146.6, 135.5, 132.1, 129.8, 129.0, 128.5, 128.0, 126.4, 118.6, 112.6, 50.9, 43.6, 42.2, 39.6, 27.9, 15.8.

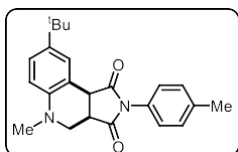
8-(tert-butyl)-5-methyl-2-phenyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (3da)



The compound was prepared according to GP-1 using 1-Phenyl-1H-pyrrole-2,5-dione (0.043 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-(4-(tert-butyl)phenyl)-*N*-methylglycinate (0.275 g, 0.75 mmol) and DIPEA (130.6 μL, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in hexane) gave **3da** as a white solid (0.048 g, 55%).

¹H NMR (500 MHz, CDCl₃) δ 7.57 (d, *J* = 2.2 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 2H), 7.38 – 7.34 (m, 1H), 7.28 (dd, *J* = 8.4, 1.1 Hz, 2H), 7.27 (d, *J* = 2.4 Hz, 1H), 6.69 (d, *J* = 8.6 Hz, 1H), 4.17 (d, *J* = 9.6 Hz, 1H), 3.59 (dd, *J* = 11.4, 2.9 Hz, 1H), 3.53 (ddd, *J* = 9.5, 4.3, 2.9 Hz, 1H), 3.12 (dd, *J* = 11.4, 4.4 Hz, 1H), 2.83 (s, 3H), 1.32 (s, 9H). ¹³C NMR (126 MHz, CDCl₃) δ 177.9, 176.0, 146.2, 142.4, 132.1, 129.1, 128.6, 127.6, 126.5, 125.5, 118.1, 112.2, 50.8, 43.6, 42.3, 39.6, 34.1, 31.5.

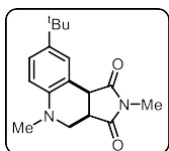
8-(Tert-butyl)-5-methyl-2-(p-tolyl)-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (3db)



The compound was prepared according to GP-1 using 1-(p-tolyl)-1H-pyrrole-2,5-dione (0.047 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-(4-(tert-butyl)phenyl)-*N*-methylglycinate (0.274 g, 0.75 mmol) and DIPEA (130.6 μL, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in hexane) gave **3db** as a white solid (0.048 g, 53%).

¹H NMR (500 MHz, CDCl₃) δ 7.57 (d, *J* = 2.2 Hz, 1H), 7.28 – 7.25 (m, 1H), 7.23 (d, *J* = 8.3 Hz, 2H), 7.17 – 7.13 (m, 2H), 6.69 (d, *J* = 8.6 Hz, 1H), 4.16 (d, *J* = 9.6 Hz, 1H), 3.58 (dd, *J* = 11.4, 2.9 Hz, 1H), 3.51 (ddd, *J* = 9.5, 4.3, 2.9 Hz, 1H), 3.11 (dd, *J* = 11.4, 4.4 Hz, 1H), 2.83 (s, 3H), 2.36 (s, 3H), 1.32 (s, 9H). ¹³C NMR (126 MHz, CDCl₃) δ 178.0, 176.1, 146.2, 142.4, 138.6, 129.7, 129.4, 127.6, 126.2, 125.4, 118.1, 112.2, 50.8, 43.5, 42.3, 39.6, 34.1, 31.5, 21.3. HRMS-ESI (*m/z*): calcd for C₂₃H₂₇N₂O₂ [M+H]⁺ 363.2067; found 363.2062.

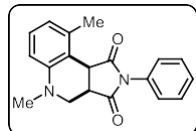
8-(Tert-butyl)-2,5-dimethyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (3do)



The compound was prepared according to GP-1 using 1-Methyl-1H-pyrrole-2,5-dione (0.028 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-(4-(tert-butyl)phenyl)-*N*-methylglycinate (0.274 g, 0.75 mmol) and DIPEA (130.6 μL, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in hexane) gave **3do** as a white solid (0.054 g, 75%).

¹H NMR (500 MHz, CDCl₃) δ 7.51 (d, *J* = 2.1 Hz, 1H), 7.23 (dd, *J* = 8.5, 2.3 Hz, 1H), 6.65 (d, *J* = 8.6 Hz, 1H), 4.01 (d, *J* = 9.4 Hz, 1H), 3.51 (dd, *J* = 11.4, 2.5 Hz, 1H), 3.35 (ddd, *J* = 9.4, 4.3, 2.5 Hz, 1H), 3.02 (dd, *J* = 11.4, 4.4 Hz, 1H), 2.98 (s, 3H), 2.78 (s, 3H), 1.32 (s, 9H). **¹³C NMR (126 MHz, CDCl₃)** δ 179.0, 177.0, 146.0, 142.4, 127.4, 125.4, 118.2, 112.2, 50.5, 43.6, 42.2, 39.6, 34.1, 31.5, 25.4. **HRMS-ESI (*m/z*):** calcd for C₁₇H₂₃N₂O₂ [M+H]⁺ 287.1754; found 287.1732.

5,9-Dimethyl-2-phenyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-*c*]quinoline-1,3(2H)-dione (3ea)

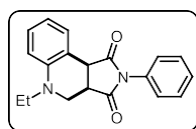


The compound was prepared according to GP-1 using 1-Phenyl-1H-pyrrole-2,5-dione (0.043 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-methyl-*N*-(*m*-tolyl)glycinate (0.243 g, 0.75 mmol) and DIPEA (130.6 μL, 0.75 mmol).

Purification by column chromatography (20% ethyl acetate in hexane) gave **3ea** as a white solid (0.042 g, 55%).

¹H NMR (500 MHz, CDCl₃) δ 7.44 (t, *J* = 7.7 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.32 – 7.26 (m, 2H), 7.13 (t, *J* = 7.9 Hz, 1H), 6.82 (d, *J* = 7.5 Hz, 1H), 6.64 (d, *J* = 8.2 Hz, 1H), 4.53 (d, *J* = 9.8 Hz, 1H), 3.59 (dd, *J* = 11.4, 1.4 Hz, 1H), 3.54 (ddd, *J* = 9.8, 4.8, 1.4 Hz, 1H), 2.96 (dd, *J* = 11.4, 4.8 Hz, 1H), 2.79 (s, 3H), 2.59 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 178.7, 175.8, 150.2, 138.7, 132.2, 129.1, 128.6, 128.1, 126.5, 122.8, 119.6, 110.7, 52.6, 44.9, 40.0, 39.6, 20.5.

5-Ethyl-2-phenyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-*c*]quinoline-1,3(2H)-dione (3fa)

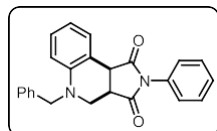


The compound was prepared according to GP-1 using 1-Phenyl-1H-pyrrole-2,5-dione (0.043 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-ethyl-*N*-phenylglycinate (0.243 g, 0.75 mmol) and DIPEA (130.6 μL, 0.75 mmol).

Purification by column chromatography (20% ethyl acetate in hexane) gave **3fa** as a white solid (0.052 g, 68%).

¹H NMR (500 MHz, CDCl₃) δ 7.52 (d, *J* = 7.1 Hz, 1H), 7.45 – 7.41 (m, 2H), 7.38 – 7.33 (m, 1H), 7.26 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.23 – 7.18 (m, 1H), 6.86 (td, *J* = 7.5, 1.0 Hz, 1H), 6.77 (d, *J* = 8.2 Hz, 1H), 4.14 (d, *J* = 9.5 Hz, 1H), 3.65 (dd, *J* = 11.6, 2.9 Hz, 1H), 3.55 (ddd, *J* = 9.5, 4.2, 3.0 Hz, 1H), 3.38 – 3.23 (m, 2H), 3.17 (dd, *J* = 11.6, 4.3 Hz, 1H), 1.18 (t, *J* = 7.1 Hz, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 177.9, 175.9, 147.3, 132.1, 130.8, 129.1, 128.7, 128.6, 126.4, 119.1, 118.6, 112.6, 47.2, 44.8, 44.0, 42.4, 10.9.

5-Benzyl-2-phenyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-*c*]quinoline-1,3(2H)-dione (3ga)

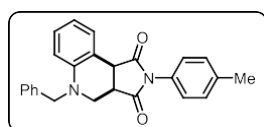


The compound was prepared according to GP-1 using 1-Phenyl-1H-pyrrole-2,5-dione (0.043 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-phenethyl-*N*-phenylglycinate (0.300 g, 0.75 mmol) and DIPEA (130.6 μL, 0.75 mmol).

Purification by column chromatography (20% ethyl acetate in hexane) gave **3ga** as a white solid (0.042 g, 53%).

¹H NMR (500 MHz, CDCl₃) δ 7.54 (d, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.29 (dd, *J* = 10.5, 3.4 Hz, 4H), 7.24 (s, 3H), 7.18 – 7.10 (m, 1H), 6.89 (t, *J* = 7.4 Hz, 1H), 6.74 (d, *J* = 8.2 Hz, 1H), 4.48 (d, *J* = 15.3 Hz, 1H), 4.28 (d, *J* = 15.3 Hz, 1H), 4.19 (d, *J* = 9.5 Hz, 1H), 3.69 (dd, *J* = 11.7, 2.8 Hz, 1H), 3.55 (ddd, *J* = 9.5, 4.2, 2.9 Hz, 1H), 3.27 (dd, *J* = 11.7, 4.4 Hz, 1H). **¹³C NMR (126 MHz, CDCl₃)** δ 177.6, 175.9, 147.6, 137.8, 132.1, 130.6, 129.2, 128.72, 128.70, 127.5, 127.4, 126.4, 119.8, 119.0, 113.5, 55.5, 49.1, 44.2, 42.5.

5-benzyl-2-(*p*-tolyl)-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-*c*]quinoline-1,3(2H)-dione (3gb)

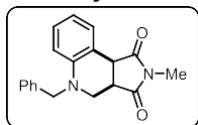


The compound was prepared according to GP-1 using 1-(*p*-tolyl)-1H-pyrrole-2,5-dione (0.047 g, 0.25 mmol), 1,3-dioxoisindolin-2-yl *N*-phenethyl-*N*-phenylglycinate (0.300 g, 0.75 mmol) and DIPEA (130.6 μL, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in hexane) gave **3gb** as a white solid (0.042 g, 55%).

¹H NMR (500 MHz, CDCl₃) δ 7.54 (d, *J* = 7.1 Hz, 1H), 7.28 (dd, *J* = 8.1, 2.3 Hz, 4H), 7.25 (d, *J* = 4.6 Hz, 3H), 7.16 (d, *J* = 8.3 Hz, 2H), 7.15 – 7.10 (m, 1H), 6.89 (td, *J* = 7.5, 0.8 Hz, 1H), 6.73 (d, *J* = 8.2 Hz, 1H), 4.47 (d, *J* = 15.3 Hz, 1H), 4.28 (d, *J* = 15.3 Hz, 1H), 4.19 (d, *J* = 9.5 Hz, 1H), 3.69 (dd, *J* = 11.7, 2.8 Hz, 1H), 3.55 (ddd, *J* = 9.5, 4.3, 2.9 Hz, 1H), 3.27 (dd, *J* = 11.7, 4.4 Hz, 1H), 2.38 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 177.7, 176.0, 147.6, 138.7, 137.8, 130.6, 129.8, 129.5, 128.7, 128.6, 127.5, 127.4, 126.2, 119.8, 119.1, 113.6, 55.5, 49.2, 44.2, 42.5, 21.3. **HRMS-ESI (*m/z*)**: calcd for C₂₅H₂₃N₂O₂ [M+H]⁺ 383.1754; found 383.1759.

5-Benzyl-2-methyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (3go)

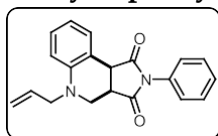


The compound was prepared according to GP-1 using 1-Methyl-1H-pyrrole-2,5-dione (0.028 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-phenethyl-*N*-phenylglycinate (0.300 g, 0.75 mmol) and DIPEA (130.6 μL, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in hexane) gave

3go as a white solid (0.057 g, 45%).

¹H NMR (500 MHz, CDCl₃) δ 7.50 (d, *J* = 7.1 Hz, 1H), 7.33 – 7.28 (m, 2H), 7.25 (s, 1H), 7.19 (d, *J* = 7.0 Hz, 2H), 7.16 – 7.08 (m, 1H), 6.87 (td, *J* = 7.5, 1.0 Hz, 1H), 6.71 (d, *J* = 8.0 Hz, 1H), 4.43 (d, *J* = 15.3 Hz, 1H), 4.24 (d, *J* = 15.3 Hz, 1H), 4.03 (d, *J* = 9.3 Hz, 1H), 3.58 (dd, *J* = 11.8, 2.7 Hz, 1H), 3.38 (ddd, *J* = 9.3, 4.3, 2.8 Hz, 1H), 3.18 (dd, *J* = 11.8, 4.4 Hz, 1H), 3.02 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 178.5, 177.0, 147.5, 137.7, 130.5, 128.7, 128.6, 127.6, 127.4, 119.7, 118.9, 113.4, 55.3, 48.5, 44.1, 42.3, 25.4. **HRMS-ESI (*m/z*)**: calcd for C₁₉H₁₉N₂O₂ [M+H]⁺ 307.1441; found 307.1441.

5-Allyl-2-phenyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (3ha)

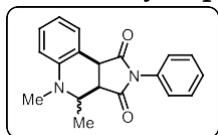


The compound was prepared according to GP-1 using 1-Phenyl-1H-pyrrole-2,5-dione (0.043 g, 0.25 mmol), 1,3-Dioxoisindolin-2-yl *N*-allyl-*N*-phenylglycinate (0.252 g, 0.75 mmol) and DIPEA (130.6 μL, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in hexane) gave

3ha as a white solid (0.072 g, 90%) and obtained characterization data were in alignment with the literature reported data.³

¹H NMR (500 MHz, CDCl₃) δ 7.53 (d, *J* = 7.2 Hz, 1H), 7.46 – 7.41 (m, 2H), 7.36 (ddd, *J* = 7.5, 3.8, 1.1 Hz, 1H), 7.27 – 7.25 (m, 2H), 7.23 – 7.17 (m, 1H), 6.89 (td, *J* = 7.5, 0.9 Hz, 1H), 6.78 (d, *J* = 8.2 Hz, 1H), 5.87 (ddt, *J* = 16.1, 10.4, 5.8 Hz, 1H), 5.29 – 5.22 (m, 2H), 4.16 (d, *J* = 9.5 Hz, 1H), 3.89 (dd, *J* = 15.6, 5.6 Hz, 1H), 3.78 (dd, *J* = 15.6, 5.9 Hz, 1H), 3.68 (dd, *J* = 11.8, 2.8 Hz, 1H), 3.55 (ddd, *J* = 9.5, 4.2, 2.9 Hz, 1H), 3.15 (dd, *J* = 11.8, 4.3 Hz, 1H). **¹³C NMR (126 MHz, CDCl₃)** δ 177.7, 175.9, 147.4, 133.3, 132.1, 130.7, 129.1, 128.67, 128.66, 126.4, 119.6, 118.8, 118.2, 113.2, 53.6, 47.8, 44.1, 42.4.

4,5-dimethyl-2-phenyl-3a,4,5,9b-tetrahydro-1H-pyrrolo[3,4-c]quinoline-1,3(2H)-dione (3ia)



The compound was prepared according to GP-1 using 1-Phenyl-1H-pyrrole-2,5-dione (0.043 g, 0.25 mmol), 1,3-dioxoisindolin-2-yl *N*-methyl-*N*-phenylalaninate (0.243 g, 0.75 mmol) and DIPEA (130.6 μL, 0.75 mmol). Purification by column chromatography (20% ethyl acetate in hexane) gave

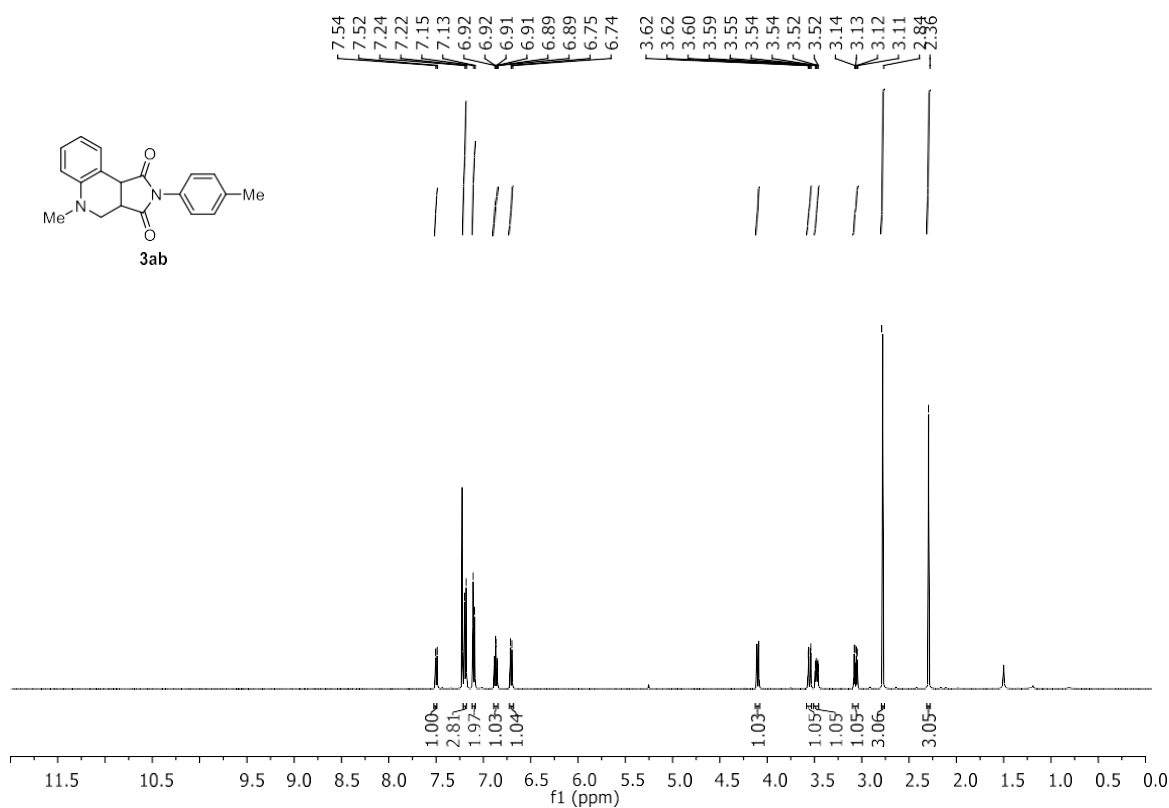
3ia as a white solid (0.040 g, 52%).

¹H NMR (500 MHz, CDCl₃) δ 7.49 (d, *J* = 7.3 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.34 (t, *J* = 7.2 Hz, 1H), 7.22 (dd, *J* = 15.9, 8.1 Hz, 3H), 6.85 (t, *J* = 7.5 Hz, 1H), 6.63 (d, *J* = 8.1 Hz, 1H), 4.13 (d, *J* = 9.4 Hz, 1H), 4.07 – 4.01 (m, 1H), 3.33 (d, *J* = 9.3 Hz, 1H), 2.82 (s, 3H), 1.08 (d, *J* = 6.7 Hz, 3H).

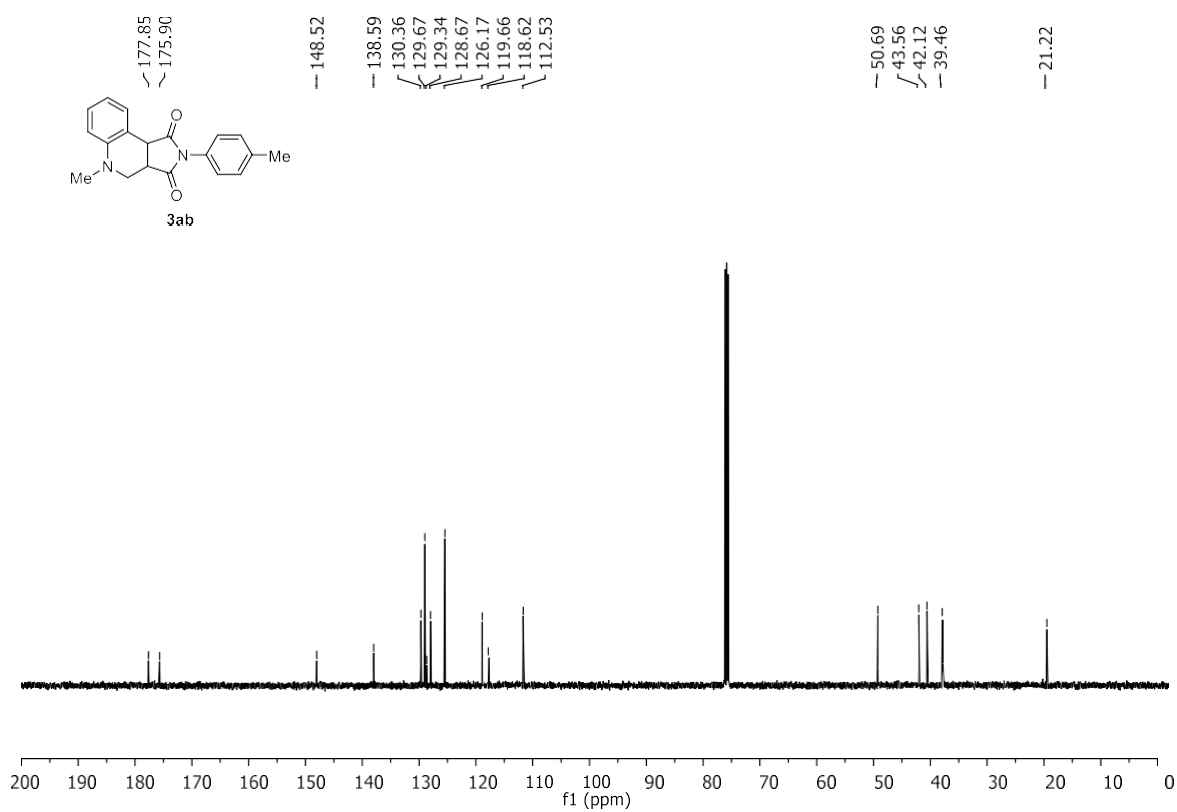
¹³C NMR (126 MHz, CDCl₃) δ 177.4, 175.9, 145.1, 132.0, 129.7, 128.9, 128.96, 128.44, 126.3, 118.9, 117.8, 113.2, 54.2, 49.5, 40.8, 37.5, 13.2. **HRMS-ESI (*m/z*)**: calcd for C₁₉H₁₉N₂O₂ [M+H]⁺ 307.1447; found 307.1443.

2.4 NMR Spectra of Compounds

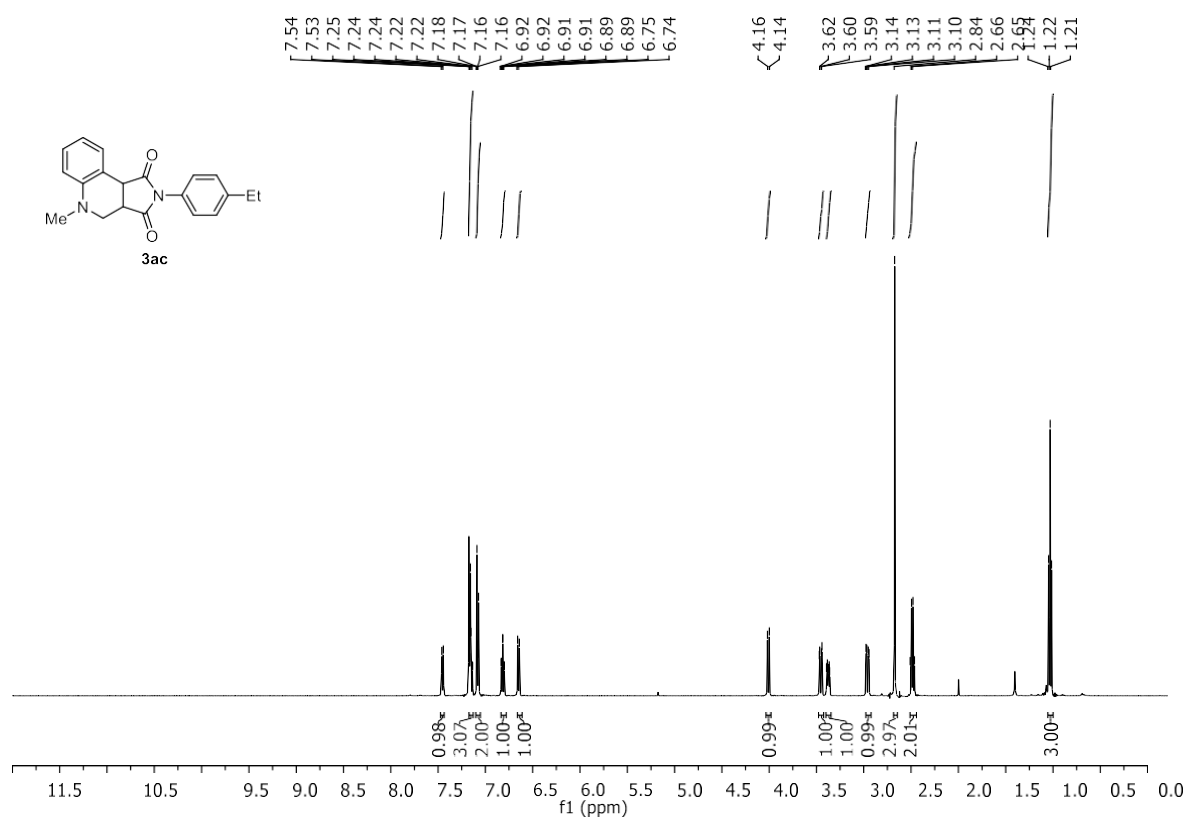
2.4.1 ^1H NMR spectrum of 3ab (CDCl_3 , 500 MHz)



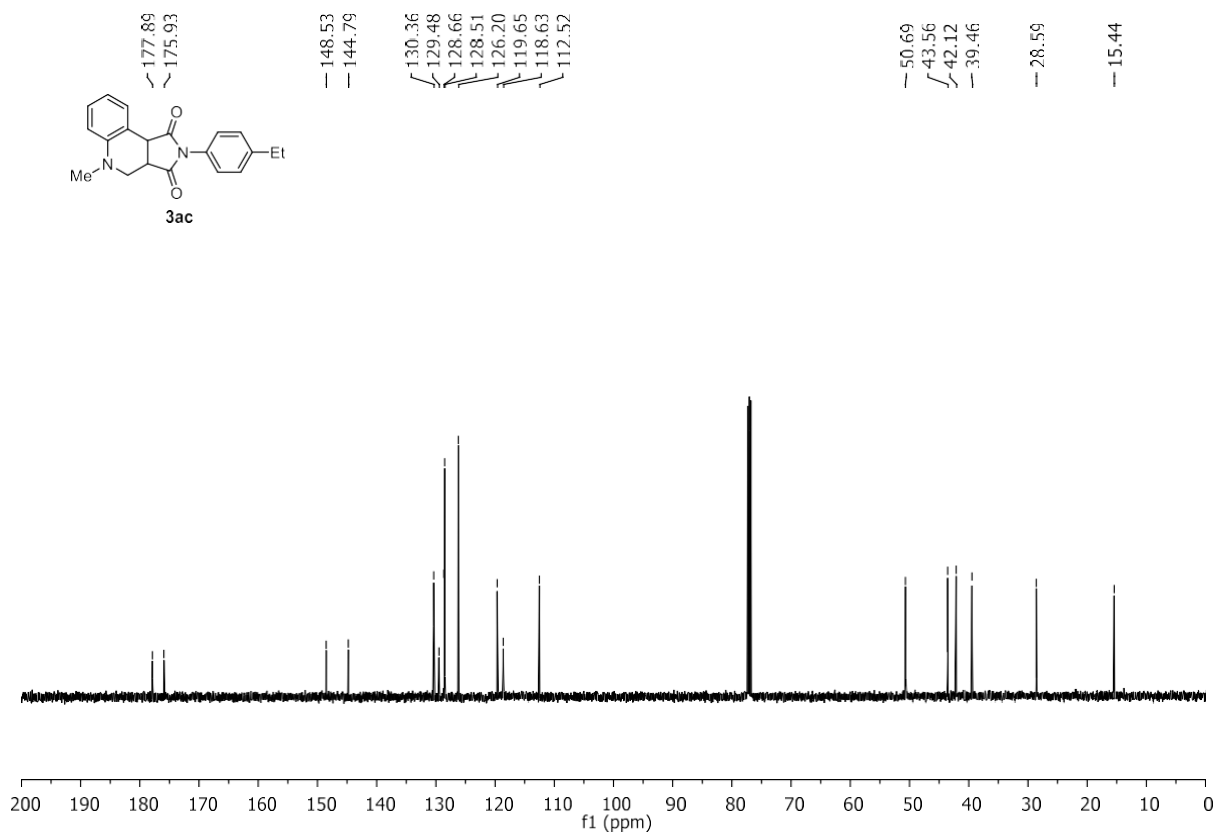
2.4.1 ^{13}C NMR spectrum of 3ab (CDCl_3 , 126 MHz)



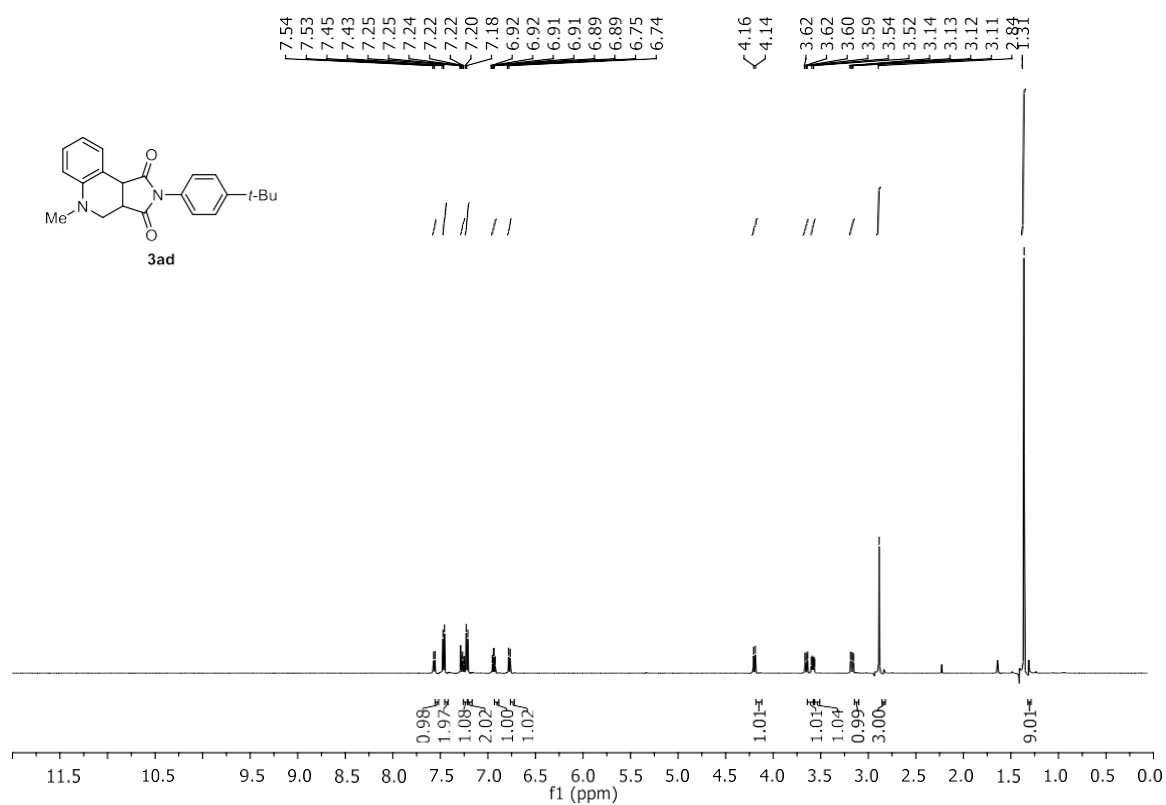
2.4.2 ¹H NMR spectrum of 3ac (CDCl₃, 500 MHz)



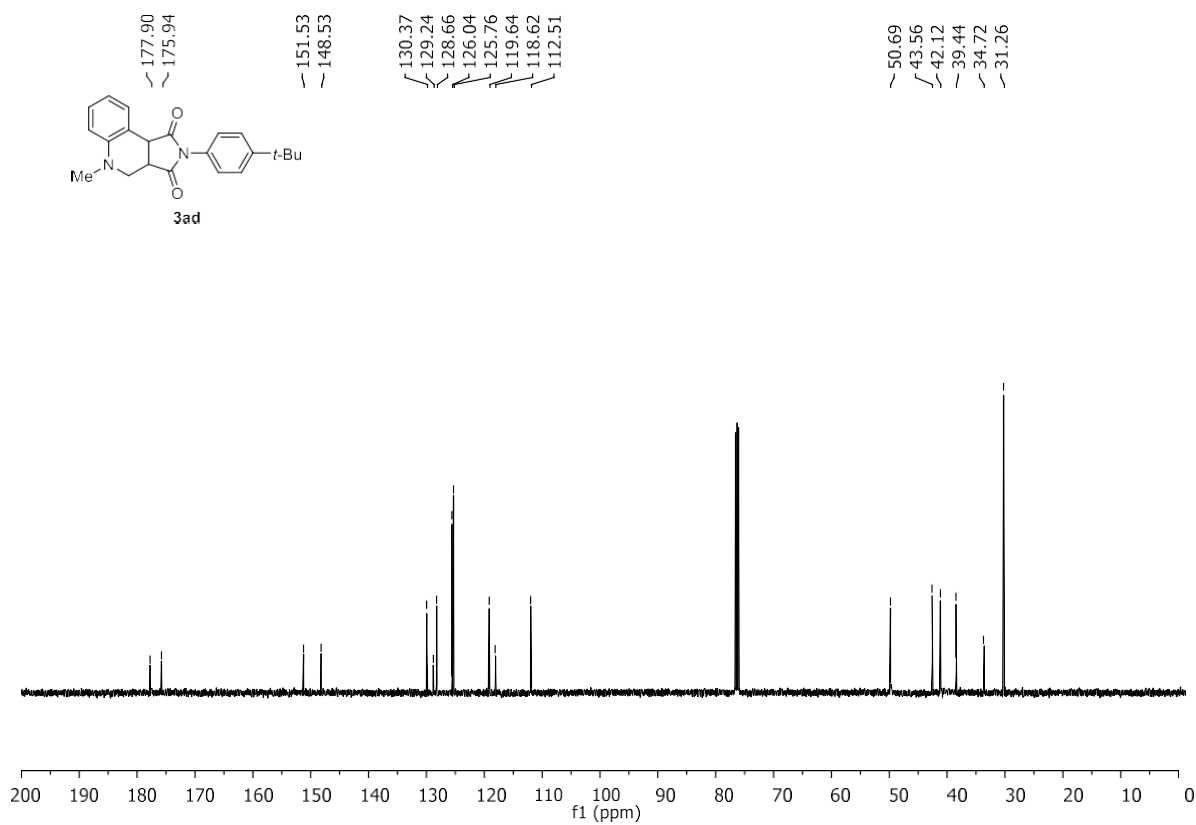
2.4.2 ¹³C NMR spectrum of 3ac (CDCl₃, 126 MHz)



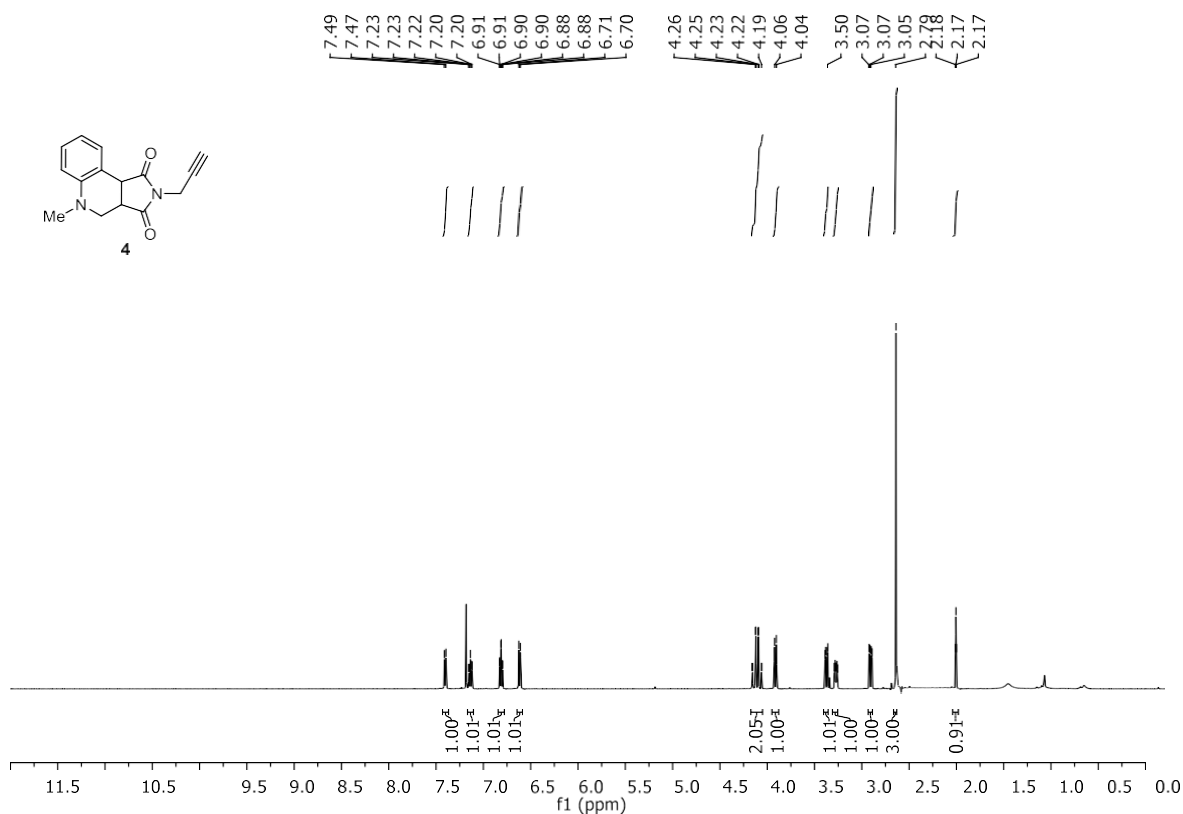
2.4.3 ^1H NMR spectrum of 3ad (CDCl_3 , 500 MHz)



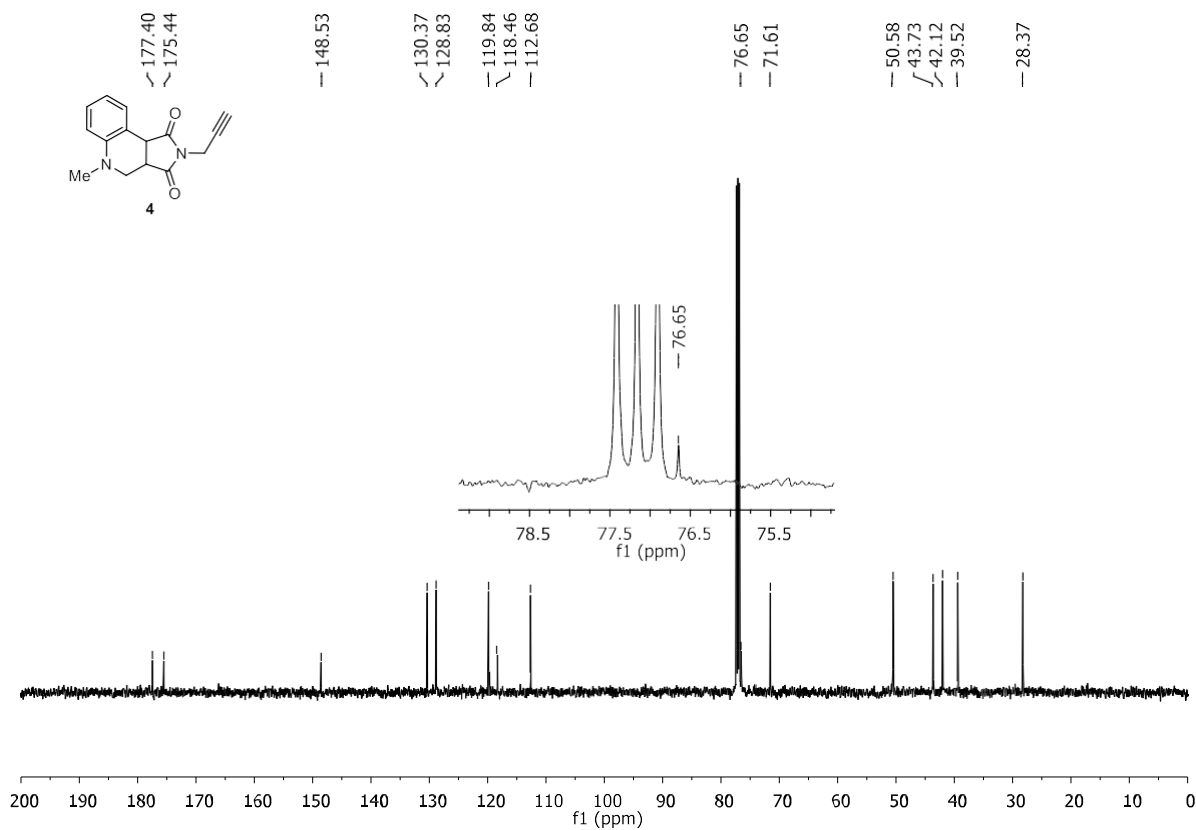
2.4.3 ^{13}C NMR spectrum of 3ad (CDCl_3 , 126 MHz)



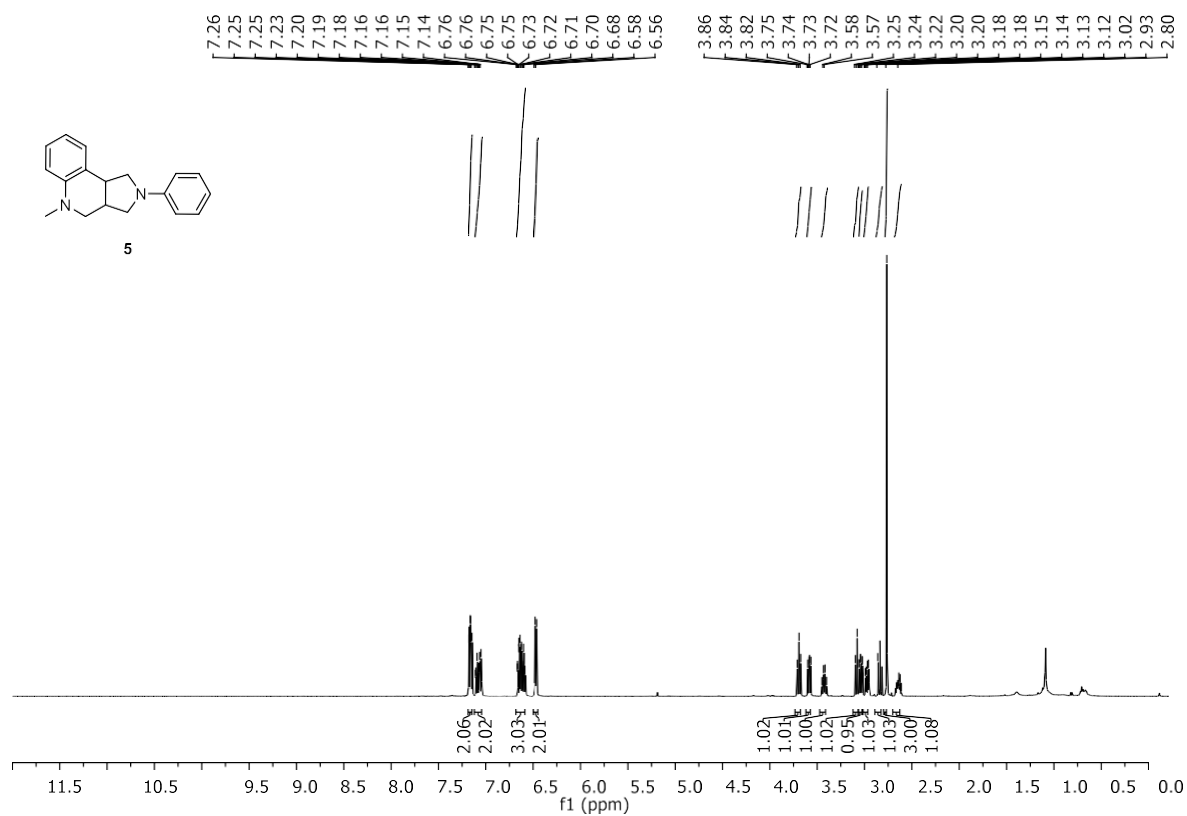
2.4.4 ¹H NMR spectrum of 4 (CDCl₃, 500 MHz)



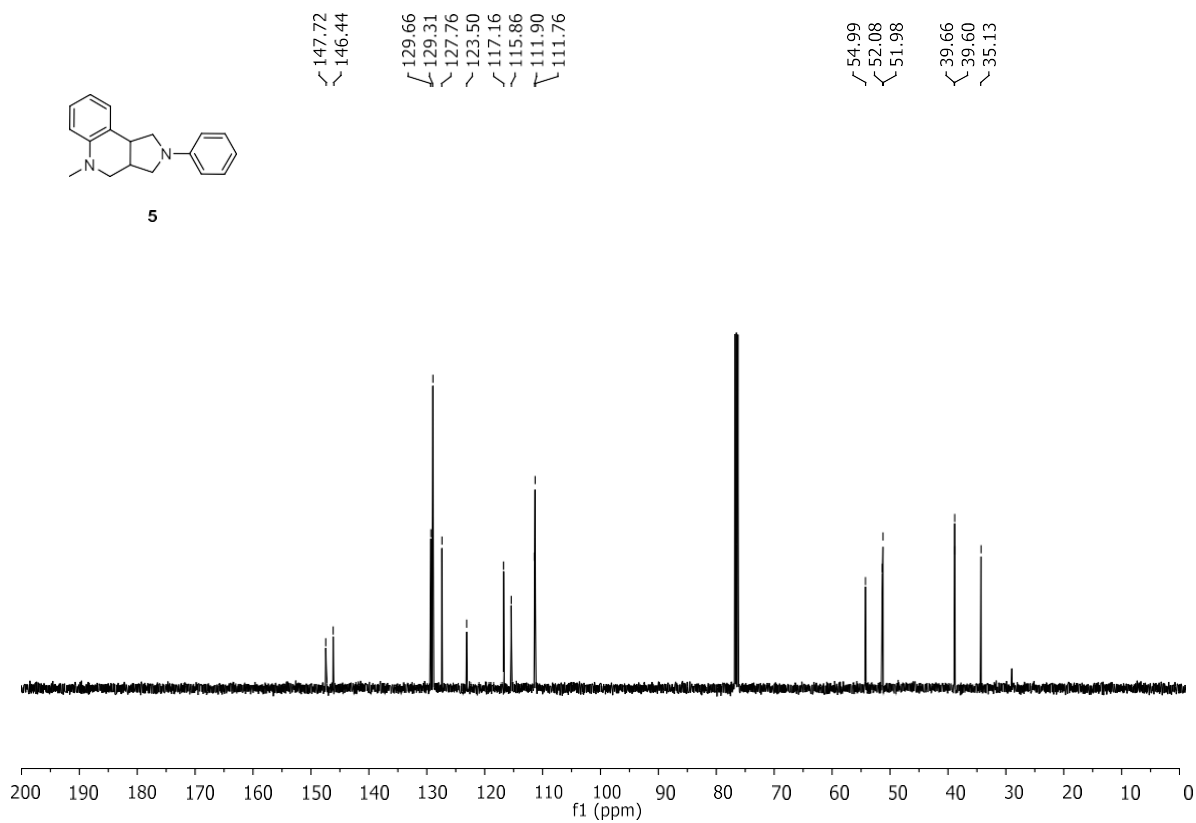
2.4.4 ¹³C NMR spectrum of 4 (CDCl₃, 126 MHz)



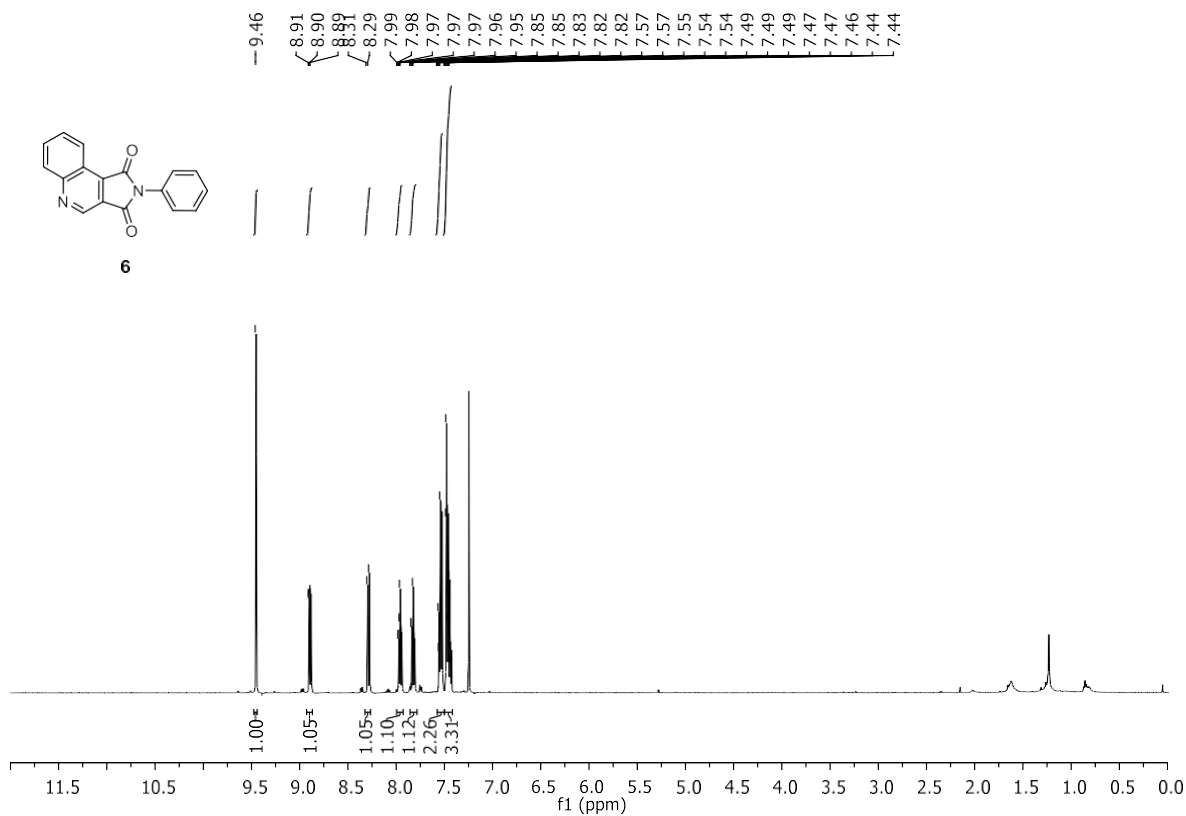
2.4.5 ^1H NMR spectrum of **5** (CDCl_3 , 500 MHz)



2.4.5 ^{13}C NMR spectrum of **5** (CDCl_3 , 126 MHz)



2.4.6 ^1H NMR spectrum of 6 (CDCl_3 , 500 MHz)



2.4.6 ^{13}C NMR spectrum of 6 (CDCl_3 , 126 MHz)

