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Synthesis and characterisation of novel fluorescent imides by a rhodium(III)-catalysed C-H activation/annulation cascade

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Dedicated to our friend and colleague Professor Sam Zard in recognition of his many outstanding contributions to science

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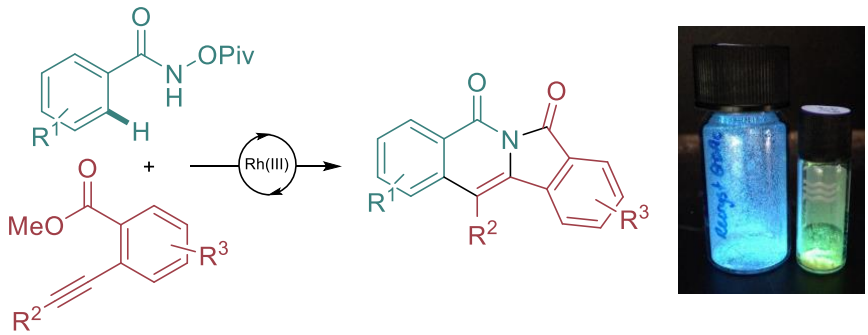
Abstract

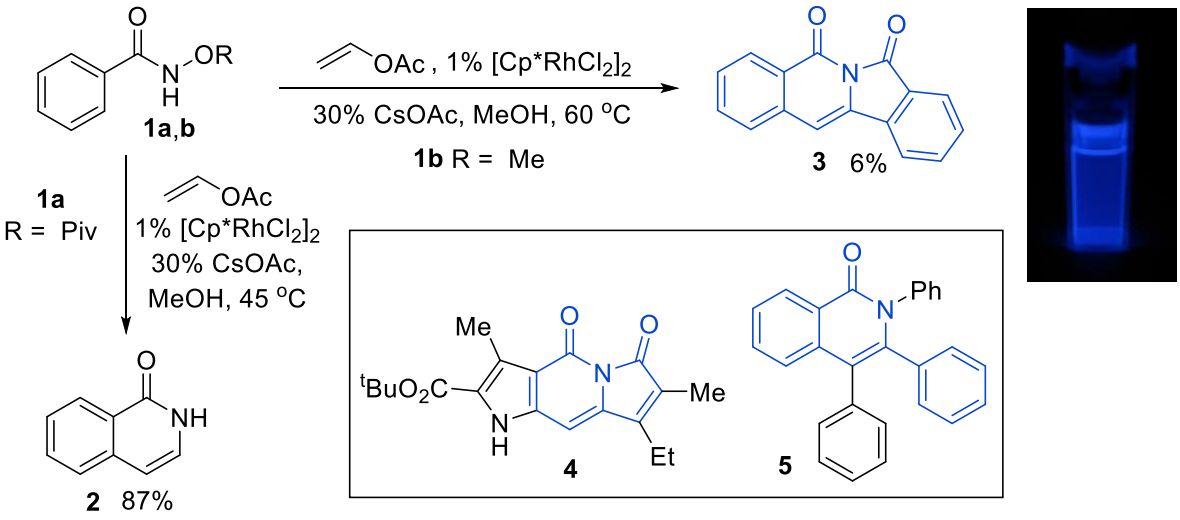
Regioselective rhodium(III)-catalysed C-H activation/annulation of *O*-pivaloyl benzoylhydroxamates with *ortho*-alkynylbenzoate esters facilitates the rapid preparation of a novel class of fluorophores based on the isoindolo[2,1-*b*]isoquinoline-5,7-dione core. The photophysical, electrochemical and coordination properties of these novel structures are investigated.



Keywords: Fluorescence, C-H activation, rhodium catalysis, heterocycles.

Introduction

Fused aromatic and heteroaromatic skeleta are integral components of a vast number of effect chemicals, from pharmaceuticals and agrochemicals to fluorescent dyes and photovoltaic materials. In recent years, selective and efficient metal-catalysed C-H activation/annulation reactions have emerged as a powerful method for the rapid assembly of complex fused skeleta from simpler mono- or acyclic precursors.[1-3] We[4,5] and others[6-12] have previously reported investigations into the use of vinyl acetate as an acetylene equivalent, for example in rhodium(III)-catalysed C-H activation/annulation processes.[4,5] During the development of a method to synthesise 3,4-unsubstituted isoquinolinones by reaction of vinyl acetate with various benzoylhydroxamates,[4] we found that while the *O*-pivaloyl benzoylhydroxamate (**1a**) gave a good yield of isoquinolinone (**2**), the corresponding *N*-methoxybenzamide **1b** gave none of the desired product **2**, instead undergoing an unexpected condensation with vinyl acetate to deliver the 2:1 adduct **3** in low yield (Scheme 1).



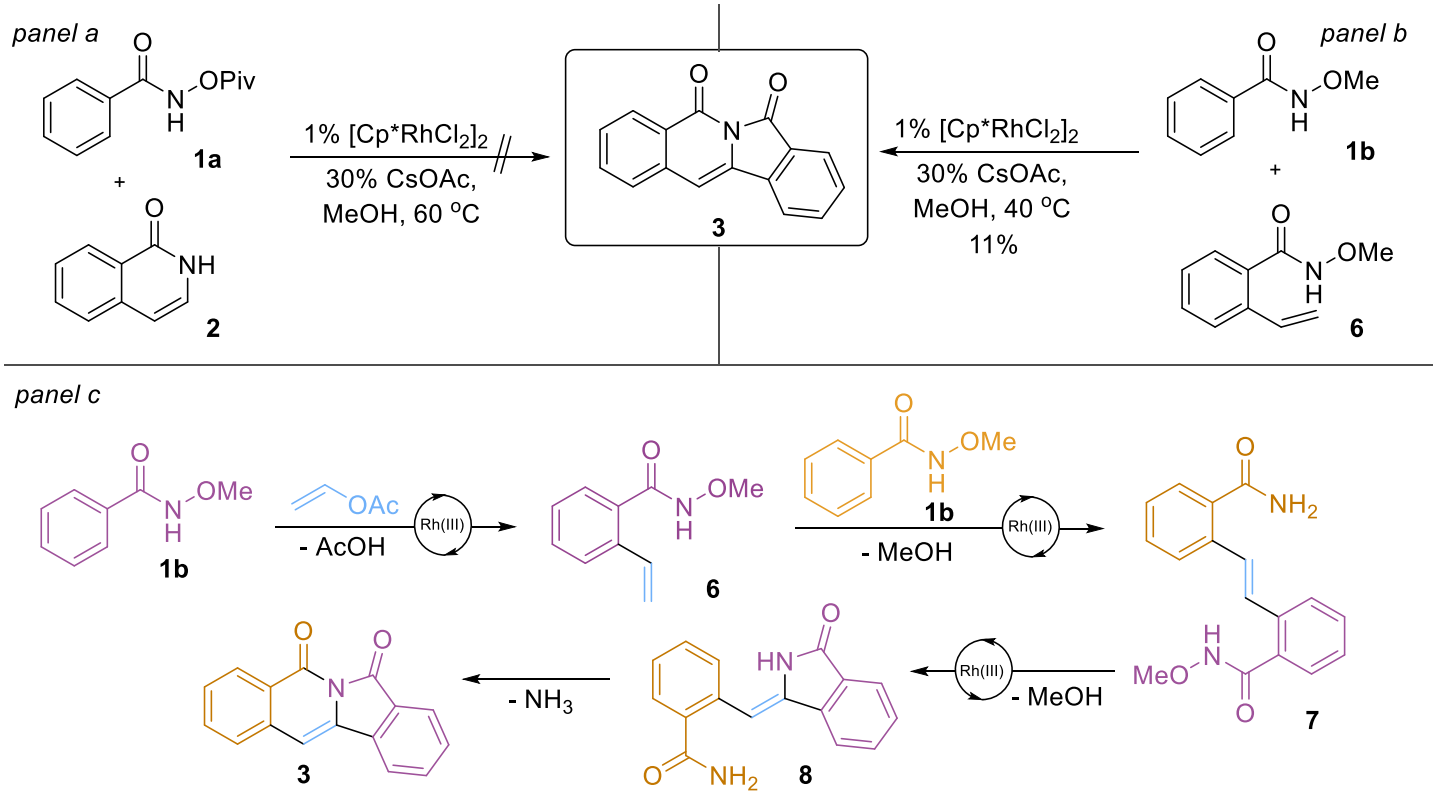
Scheme 1. Adventitious synthesis of fluorescent heterocycle **3** and similarity to previously reported fluorophores **4** and **5**.

Compound **3** exhibited strong blue fluorescence when irradiated with UV light (λ_{abs} 375 nm, λ_{emis} 413 nm). Although compound **3** has been known for well over 100 years[13] and various synthetic approaches to this general framework have been reported,[14-19] the photophysical properties of this class of heterocycles have not been investigated in depth. Interestingly, however, the tetracyclic core of **3** has clear structural similarities with known fluorophores such as the isodipyrrinones exemplified by **4**[20,21] and polyarylated isoquinolinones such as **5**.[22] As such, we wished to further investigate the synthesis and properties of diverse substituted variants of **3**, and report herein the development of a general and convergent strategy for their preparation, along with studies of their photophysical, electrochemical and coordination behaviour.

Results and Discussion

Our first task was to develop a synthetically-useful and generalised approach to functionalised derivatives of **3**, and we began by investigating its opportunistic formation under the conditions outlined in Scheme 1. We

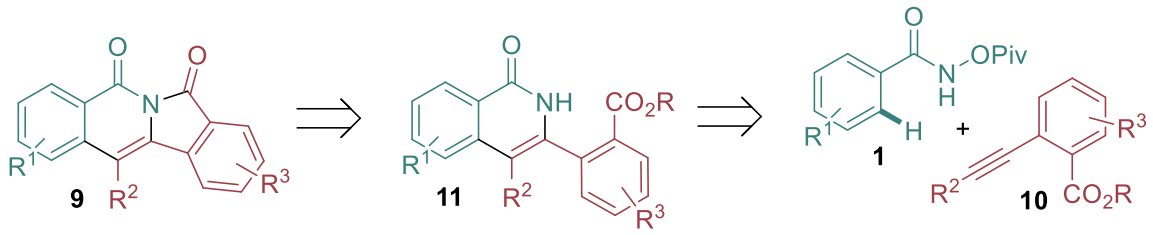
considered that **3** might potentially arise by transient formation of isoquinolinone (**2**) and subsequent annulation of a second equivalent of benzoyl hydroxamate; however, attempted coupling of **2** with even the more reactive **1a** failed to produce compound **3** (Scheme 2, panel a). We next considered whether the reaction might proceed through formation of *o*-styryl hydroxamate **6**: vinyl acetate has been demonstrated to act as a vinylating reagent under certain conditions of rhodium-catalysed C-H activation,[23-25] and Glorius has demonstrated the directed C-H olefination of *N*-methoxybenzamides such as **1b** with styrenes.[26] In the event, reaction of compounds **1b** and **6**[27] gave an 11% isolated yield of **3** (Scheme 2, panel b). A proposed pathway for the formation of **3** is shown in Scheme 2, panel c. Vinylation of **1b** with vinyl acetate produces substituted styrene **6**, which reacts with further **1b** to produce the stilbene **7**. The precise pathway from **7** to **3** is not known but we propose that vinylic C-H activation and cyclisation could give isoindolinone **8**, which would then undergo condensation with elimination of ammonia to generate **3**: Glorius has previously reported formation of isoindolinones through C-H activation/oxidative cyclisation of styrenic benzamides under closely related conditions.[28] Interestingly, during attempts to optimise the formation of **3**, we observed the precipitation of a highly insoluble material which, although impure, gave ^{1}H NMR data in d_6-DMSO which was consistent with structure **7**. Although the material could not be redissolved in methanol, heating in this solvent in a sealed microwave vessel with $[Cp^*RhCl_2]_2$ and caesium acetate at 80 °C led to formation of **3**, supporting the notion that this material is an intermediate.



Scheme 2. Mechanistic investigations and proposed pathway for the formation of **3**.

Despite improved understanding of the origins of **3**, we did not feel that this approach would ultimately prove useful in the synthesis of analogues. Ideally, our approach should allow ready and independent variation of substituents around each of the benzene rings, and additionally we wished to address the poor solubility of **3** by attachment of solubilising alkyl groups to the rigid heteroaromatic framework. However, we remained

attracted by the convergence of rhodium(III)-catalysed C-H activation/annulation as a method for assembling the targets **9**,[22,29] and proposed a new approach outlined in Scheme 3.



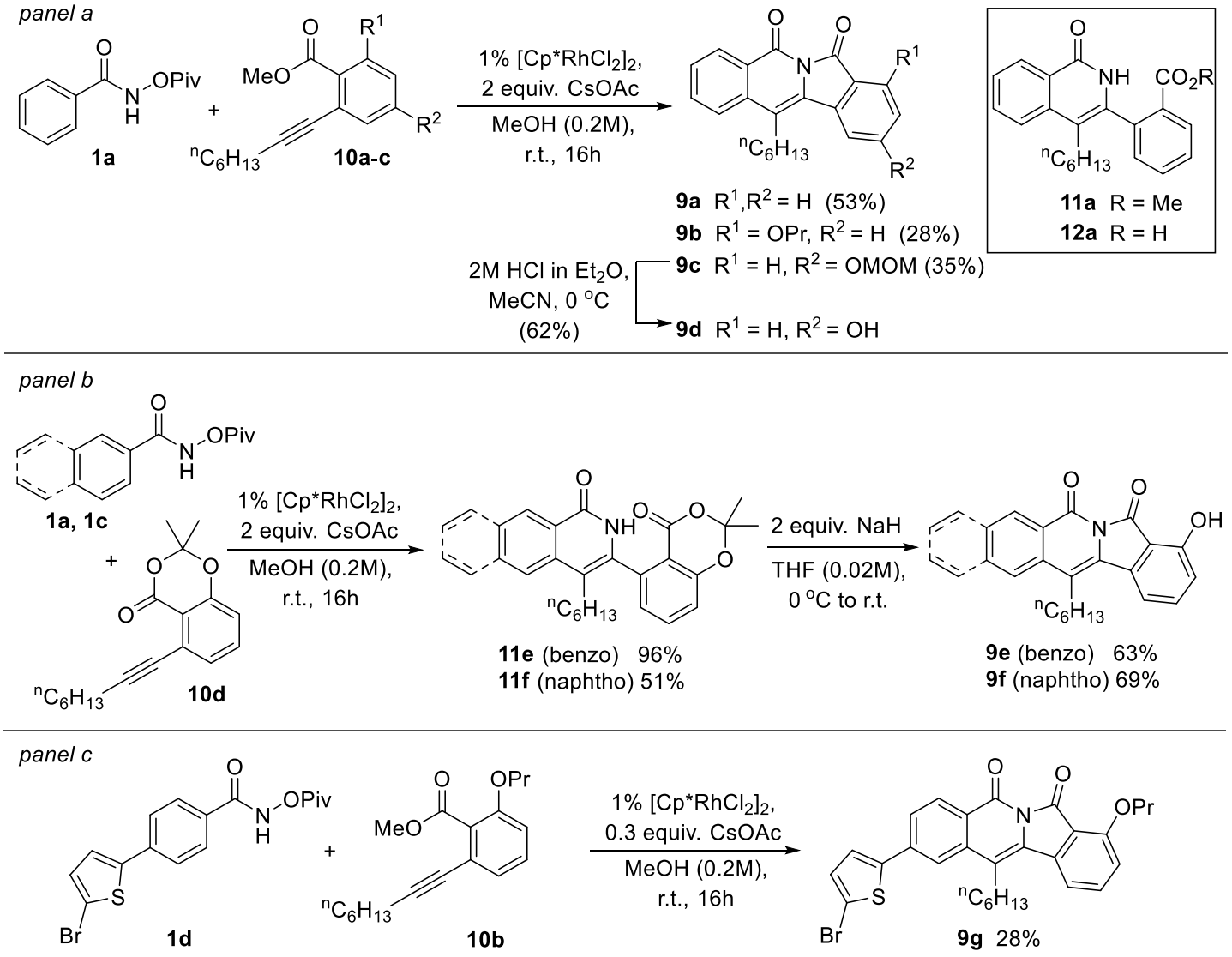
Scheme 3. Proposed convergent synthesis of substituted fluorescent imides **9**.

We recognised that cyclometallation of activated benzoylhydroxamates **1** could initiate a regioselective annulation with readily-prepared *ortho*-alkynylbenzoate esters **10** to generate isoquinolinones **11**; condensation of the isoquinolinone nitrogen with the ester (potentially in the same operation) would then generate the targets **9**. The success of this strategy depends upon a regioselective outcome in the rhodium-catalysed annulation of **1** with non-symmetrical alkynes, but we were encouraged at the outset that Fagnou had reported that aryl/alkyl-substituted alkynes do indeed preferentially generate the 3-aryl,4-alkylisoquinolones on reaction with compounds of type **1**, albeit that they had not investigated the impact of *ortho*-aryl substituents on the reactions.[30,31] We note that, subsequent to our own studies, the groups of both Guo and Fan[18] and Wang[19] have utilised rhodium(III)-catalysed annulation followed by (respectively) palladium-catalysed oxidative carbonylations/carboxylations to generate the five-membered ring of the imide in compounds related to **9**.

Our initial investigations involved the reaction of *O*-pivaloyl benzoylhydroxamate (**1a**) with methyl 2-(oct-1-yn-1yl)benzoate (**10a**) (Scheme 4, panel a). Under conditions analogous to those reported by Fagnou,[30] we were pleased to observe the direct formation of the desired imide **9a** as a ca. 1:1 mixture with the uncyclised amidoester **11a** by analysis of the ^{1}H NMR of the crude reaction mixture; pleasingly, no traces of regioisomeric annulation products could be observed. Attempted purification by column chromatography was complicated by partial hydrolysis of the imide to amido acid **12a** and so the product was instead isolated by precipitation from the crude reaction mixture by addition of ethereal HCl, followed by crystallisation from ethyl acetate to give a 53% yield of pure **5a**. Since sufficient quantities of material for investigation of the photophysical properties were readily prepared by this method, further optimisation was not undertaken for this or subsequent products.

We next investigated the effect of introducing electron-donating oxygen substituents to the aromatic ring of the isoindolinone subunit. The 2-propyloxy-substituted ester **10b** underwent cyclisation under the standard conditions to give an unoptimised 28% yield of imide **9b**. Reaction of the 4-(methoxymethyloxy)-substituted ester **10c** with **1a** gave the MOM-protected imide **9c** in 35% yield; subsequent removal of the MOM-group under acidic conditions gave the free phenol **9d**. In order to introduce a free phenol *ortho*- to the indolinone carbonyl group, we used an isopropylidene group to protect both acid and phenol substituents in **10d** (Scheme 4, panel b). Annulation under the standard conditions returned the non-cyclised isoquinolone **11e** in high yield; cyclisation to the desired imide **9e** was achieved in a separate step by intramolecular acylation of the isoquinolone nitrogen under basic conditions, with concomitant loss of acetone revealing the free phenol in a single operation. The same sequence was carried out on the naphthoic acid-derived *O*-pivaloylhydroxamate **1c**, leading to imide **9f** bearing an extended π-system. Finally, we investigated extension

of conjugation through appending a thienyl substituent to the benzoylhydroxamate (Scheme 4, panel c): reaction of **1d** with alkyne **10b** gave imide **9g** in an unoptimised 28% yield. The bromine substituent in **9g** was included to facilitate the later introduction of further (hetero)biaryls through cross-coupling chemistry should this prove of interest.



Scheme 4. Synthetic routes to substituted fluorescent heterocycles **9a**-**g**.

In all, seven different imides **9a**-**g** were prepared through the C-H activation/annulation/cyclisation sequence, and we next sought to investigate their photophysical properties.

Absorption/emission studies

Electronic absorption and emission spectra of imides **9a**-**g** were recorded in dichloromethane (Figure 1 and Table 1). The quantum yields of fluorescence were calculated using 9,10-diphenylanthracene as standard since its λ_{max} of absorbance (375 nm) is close to that of imide **9a** (383 nm). Compared with the isodipyrronine **4**, imide **9a** is slightly blue-shifted in both absorption and emission spectra, with a smaller Stokes shift (15 nm *vs* 29 nm) and a slightly reduced but still relatively high quantum yield of fluorescence. Fluorescence data for

the triarylisoquinolinone **5** are only reported in the solid-state, but **9a** shows red-shifted emission by comparison. Introduction of alkoxy or hydroxyl groups to the isoindolinone rings had relatively little effect on the emission/absorption properties: *ortho*-substitution in **9b**/**9e** produces a small red shift, while the *para*-substituted products **9c**/**9d** exhibit a small blue shift; however, while the quantum yields for the *ortho*-substituted compounds were similar to **9a**, those for the *para*-substituted variants were significantly lower. Extension of the isoquinolone π-system in the naphthalene-derived **9f** led to the longest wavelength emission and absorption, giving similar results to **4** but with a stronger molar absorption. Finally, the bromothienyl product **9g** displayed similar absorption/emission wavelengths to **9a** along with strong absorbance features below 350 nm corresponding to the thienyl group, suggesting the π-systems are not strongly coupled.

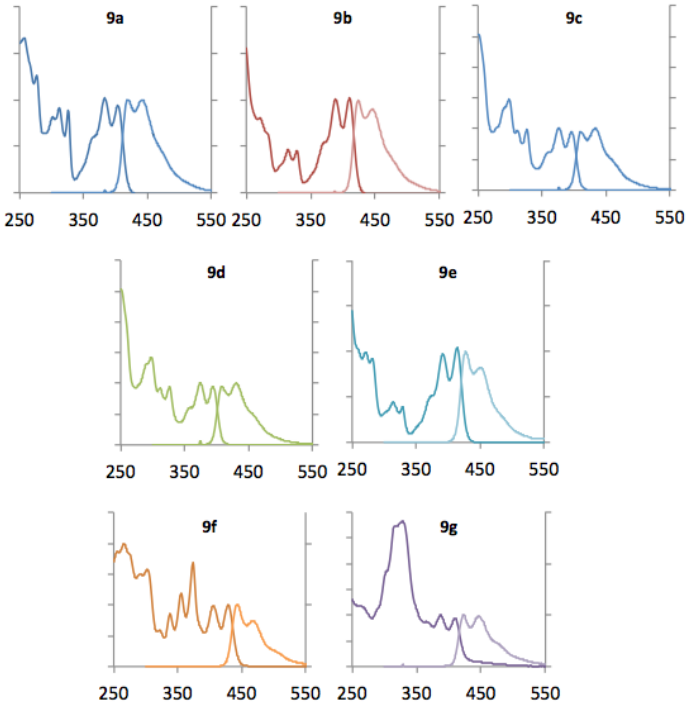


Figure 1. Absorption/emission spectra for **9a**-**9g**. Absorption maxima normalised to A = 1.0, fluorescence spectra in arbitrary units.

Table 1. Absorption and emission data for imides **9a**-**9g**

Imide	Absorbance (nm)		Fluorescence (nm)		ε^a	Φ_{rel}
9a	383[b]	403	418	439	2.34	0.44
9b	392	413[b]	427	442	2.81	0.32
9c	377[b]	398	409	433	2.51	0.17
9d	375[b]	396	407	431	2.01	0.15
9e	394	416[b]	427	449	2.68	0.45
9f	408	429[b]	441	466	3.14	0.44
9g	390[b]	408	422	446	2.07	0.15
4[c]	400[b]	424	453	- -	1.52	0.72
5[d]	- -	- -	401	414	- -	- -

[a] molar extinction coefficients reported in 10^4 $M^{-1}cm^{-1}$; [b] molar absorptivity measured at this wavelength as λ_{max}; [c] values taken from reference 20, recorded in chloroform; [d] values estimated from reference 22, recorded in the solid state.

Electrochemical studies

To further probe the substituent effects, we carried out studies of the electrochemical behaviour of imides **9a**, **9b**, and **9g** (Figure 2 and Table 2 - see SI for cyclic voltammograms of **9b** and **9g**).

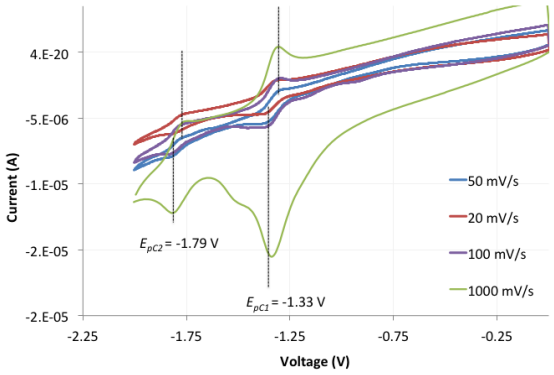


Figure 2. Cyclic voltammograms of **9a** (1.0 mM) in non-aqueous media ($CH_3CN/[^nBu_4N]BF_4$ 0.10 M).

Table 2. Reduction potentials for imides **9a**, **d**, and **g**

Entry	Imide	E_{pC1} (V)	ΔE_{pC1} (V)	E_{pC2} (V)	ΔE_{pC2} (V)
1	**9a**	-1.33	0.066	-1.79	0.048
2	**9b**	-1.38	0.053	-1.80	0.058
3	**9g**	-1.37	0.014	-1.74	0.014

All three compounds displayed two reversible reduction peaks. The presence of the electron-donating *ortho*-alkoxy substituent in **9b**/**9g** causes a small increase in the first reduction potential (entries 1 vs 2/3), while the second reduction potential does not appear influenced by the presence of the propoxy group but is sensitive to the presence of the thienyl substituent in **9g** (entries 1/2 vs entry 3). These results suggest that the 'isoindolinone' and 'isoquinolinone' portions of the molecules are behaving effectively as isolated π-systems.

Metal ion complexation

Alongside the intrinsic fluorescence properties of the imides, we were interested in exploring their behaviour as selective ligands for metal ions, and hence potentially as fluorescent sensors. We were encouraged in this direction by inspection of the high-resolution mass spectrum of **9a**, which featured a prominent peak for the $[M_2Na]^+$ ion at 685.3031 alongside the expected $[MNa]^+$ ion at 354.1459, suggesting that the imide was a reasonably strong donor ligand to the sodium cation.

We therefore conducted a complexation screen by adding various metal salts ($Cu(BF_4)_2$, $Co(BF_4)_2$, $Zn(OTf)_2$ and $Eu(OTf)_3$) to solutions of **9a** in ethyl acetate. All gave colour changes compared with the free metal salt, but the complex with $Zn(OTf)_2$ also uniquely displayed fluorescence when observed under a UV lamp at 365 nm and was selected for further study. Inspection of solutions of a 2:1 mixture of imide **9a** and $Zn(OTf)_2$ at various concentrations revealed that coordination behaviour was only observed to a significant extent at a concentration of 10^{-4} M, with solutions at 10^{-5} and 10^{-6} M showing absorption and emission behaviour identical to **9a** alone (Figure 3, panel a). This was supported by quantitative titrations using $2x10^{-4}$ M **9a** which showed bathochromic shifts in the emission λ_{max} from 440 nm to 462 nm upon addition of zinc ions, but that >2 equivalents of $Zn(OTf)_2$ were required to reach the steady state (Figure 3, panel b). Crystals of a complex between **9a** and $Zn(OTf)_2$ were grown by slow evaporation from acetone and analysis by X-ray diffraction confirmed a 2:1 complex **13** in which the 'isoquinolinone' portion of the imide remained unchanged with respect to the parent imide, but the 'indolone' portion of the imide showed C-N bond shortening/C-O bond lengthening consistent with significant electron donation to the zinc (Figure 3, panel c). A change in one of the two C=O absorbances was also observed in the infra-red spectrum of complex **13**, consistent with weakening of one of the two C=O bonds. Complex **13** shows distinct solid-state fluorescence properties to the parent **9a**. Further studies of this complexation behaviour were limited by the poor solution stability of **13**.

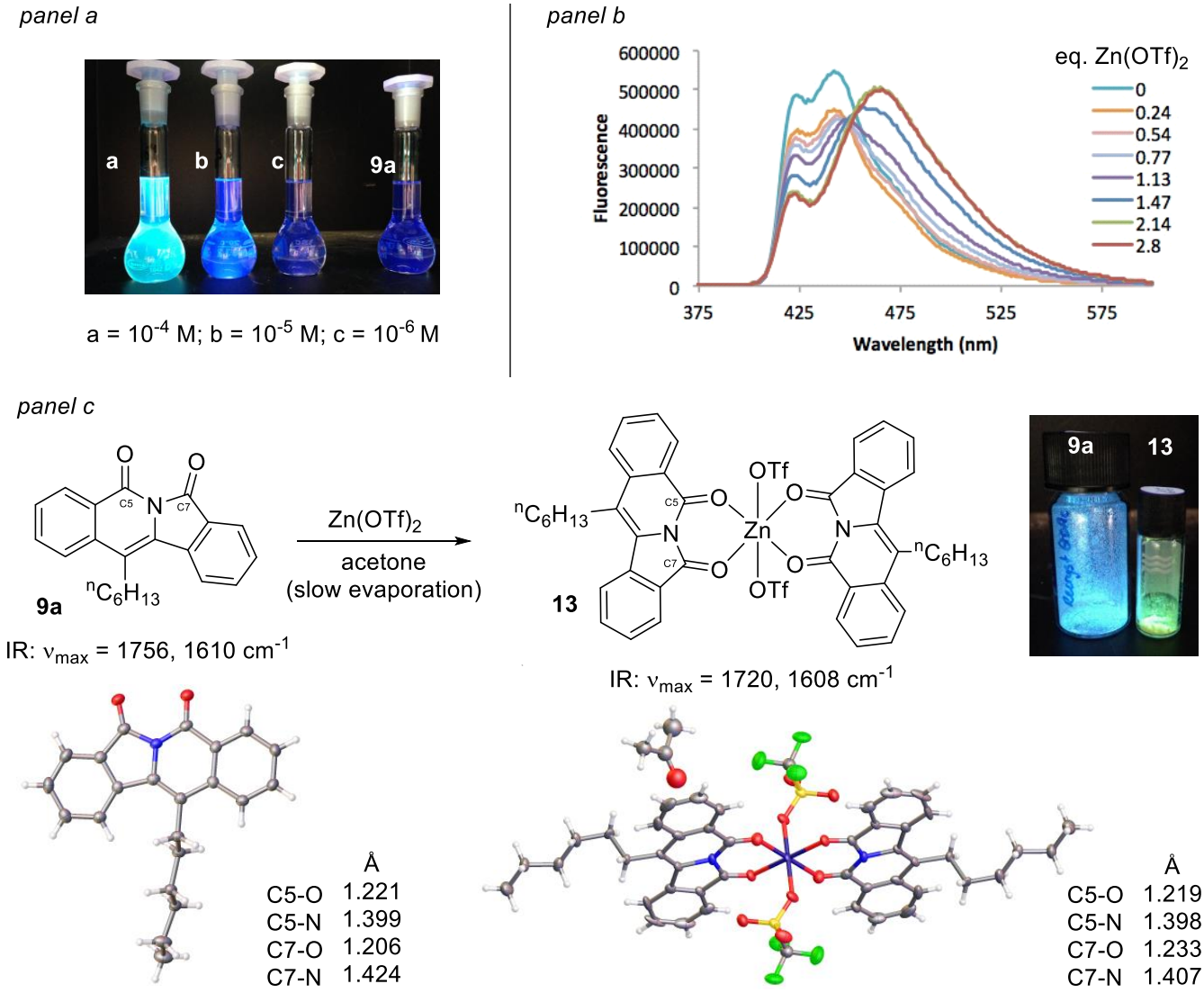


Figure 3. Panel a: fluorescence of 2:1 mixtures of **9a** and $Zn(OTf)_2$ at varying concentrations in EtOAc; panel b: fluorescence titration of **9a** (2 x 10^{-4} M in dichloromethane) and $Zn(OTf)_2$ in dichloromethane; panel c: crystallographic and IR data for **9a** and zinc complex **13**, plus solid-state fluorescence.

Conclusions

C-H Activation/annulation cascades have been employed in the synthesis of novel fluorescent isoindolo[2,1-*b*]isoquinoline-5,7-dione structures **9**. These compounds show reasonable quantum yields but narrow Stokes shifts. Attempted modulation of the absorption/emission properties met with limited success, and electrochemical studies suggest that the two 'halves' of the heterocyclic core are behaving as electronically isolated units. The behaviour of one of the imides **9a** as a ligand for zinc(II) ions was probed: while complexation could be observed spectroscopically and structurally, the assemblies were chemically rather unstable. Overall, the utility of C-H activation/annulation cascades for the rapid assembly of complex polycyclic heteroaromatic structures has been further demonstrated and this method should continue to find utility in the exploration of such scaffolds in a variety of discovery settings.

Experimental Section

General. All experiments were conducted in oven-dried glassware, under a dry nitrogen atmosphere with anhydrous solvents, unless otherwise stated. Hygroscopic caesium acetate (CsOAc) was stored in a desiccator. Anhydrous solvents were obtained from a solvent purification system. Anhydrous methanol was stored on 3Å molecular sieves. All other solvents and reagents were obtained from commercial sources and used without further purification.

Flash silica chromatography was performed using Fischer Matrix silica gel (35-70 µm particles) and thin layer chromatography was carried out using pre-coated silica plates (Merck Kieselgel 60F254). Spots were visualised using UV fluorescence (λ_{max} = 254 nm) or chemical staining with potassium permanganate. All chromatography eluents were HPLC grade and used without purification. Petrol refers to petroleum ether (b.p. 40-60°C).

Proton (^{1}H) and carbon (^{13}C{^{1}H}) nuclear magnetic resonance spectra were recorded using a Bruker DPX 300, a Bruker DRX 500 or a Bruker Avance 500 spectrometer using an internal deuterium lock. ^{1}H NMR chemical shifts (δ) are quoted in ppm downfield of tetramethylsilane or residual solvent peaks and coupling constants (*J*) are quoted in Hz. ^{13}C{^{1}H} NMR spectra were recorded with broadband proton decoupling at 75 MHz and 125 MHz. Assignments were made on the basis of chemical shift and coupling data, using COSY and DEPT where necessary. Infra-red spectra were recorded on a Perkin Elmer Spectrum One FT-IR spectrometer, with absorption reported in wavenumbers (cm^{-1}). High-resolution electrospray mass spectra (ESI-MS) were measured on a Bruker MicroTOF-Q or Bruker MaXis Impact spectrometer in positive mode. Melting points were determined using a Griffin D5 variable temperature apparatus and are uncorrected.

Synthesis

N-(Pivaloyloxy)benzamide (**1a**) and *N*-(pivaloyloxy)2-naphthamide (**1c**) were prepared according to the procedures of Liebeskind[33] and Glorius[34] respectively.

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General procedure. 12-Hexylisoindolo[2,1-*b*]isoquinoline-5,7-dione (9a). *N*-(Pivaloyloxy)benzamide (**1a**) (221 mg, 1.00 mmol), [Cp*RhCl$_2$]$_2$ (6.0 mg, 0.01 mmol), CsOAc (382 mg, 2.00 mmol) and methyl 2-(1-octynyl)benzoate (**10a**) (366 mg, 1.50 mmol) were dissolved in MeOH (5 mL, 0.2 M). The reaction was stirred at room temperature for 16 hours and concentrated *in vacuo*. The crude mixture was suspended in cold ether (0 °C) and 2M HCl in ether (5 mL) was added to the solution to precipitate the product. The solid was filtered and redissolved in $CHCl_3$. CsOAc was filtered off from the solution, which was concentrated *in vacuo* and the crude product crystallised from EtOAc. The desired imide **9a** was isolated as yellow needles (176 mg, 53%). Mp 172-175 °C (EtOAc); δ_H (300 MHz, $CDCl_3$) 8.56 (1H, d, *J* 7.9), 8.07 (1H, d, *J* 7.6), 7.90 (1H, d, *J* 7.9), 7.80-7.71 (3H, m), 7.58-7.52 (2H, m), 3.19-3.08 (2H, m), 1.75 (2H, dt, *J* 10.9, 7.3), 1.67-1.54 (2H, m), 1.49-1.31 (4H, m), 0.94 (3H, t, *J* 7.0); δ_C (75 MHz, $CDCl_3$) 165.4, 159.9, 136.6, 135.4, 135.0, 134.0, 131.1, 129.8, 129.7, 128.7, 128.5, 128.4, 126.0, 124.1, 123.8, 119.9, 31.8, 29.9, 29.2, 26.8, 22.8, 14.2; HRMS (ESI$^+$): *m/z* calculated for formula: $C_{22}H_{22}NO_2$ [MH$^+$] 332.1645; found 332.1635; IR (ν_{max}, solid, cm^{-1}): 3080, 2952, 2851, 1758, 1673, 1599, 1472, 1293, 1157, 1097, 1034.

12-Hexyl-8-propoxyisoindolo[2,1-*b*]isoquinoline-5,7-dione (9b). The desired compound was isolated as yellow needles (106 mg, 32%) from methyl 2-(oct-1-yn-1-yl)-6-propoxybenzoate (**10b**) (290 mg, 0.960 mmol, 1.10 eq.) and *N*-(pivaloyloxybenzamide) (**1a**) (192 mg, 0.870 mmol) following the general procedure. The crude reaction mixture was treated with 2N HCl in ether (1 mL) and stirred for 2 hours to convert the methyl ester to the imide. The solvent was removed *in vacuo* and the product was crystallised from cold MeOH. Mp

142-144 °C (MeOH); δ_H (500 MHz, $CDCl_3$) 8.55 (1H, dd, J 7.9, 0.8), 7.76-7.69 (2H, m), 7.63 (1H, t, *J* 8.1), 7.51 (1H, ddd, *J* 8.1, 6.7, 1.5), 7.43 (1H, d, *J* 7.8), 6.97 (1H, d, *J* 8.3), 4.13 (2H, t, *J* 6.4), 3.13-3.05 (2H, m), 2.00-1.87 (2H, m), 1.72 (2H, ddd, *J* 11.6, 10.4, 6.4), 1.64-1.54 (2H, m), 1.47-1.31 (4H, m), 1.13 (3H, t, *J* 7.4), 0.93 (3H, t, *J* 7.1); δ_C (126 MHz, $CDCl_3$) 163.2, 159.7, 159.2, 137.6, 136.6, 136.4, 133.7, 130.8, 129.7, 128.7, 128.2, 123.9, 119.3, 115.7, 115.6, 113.3, 70.8, 31.8, 29.9, 29.1, 26.7, 22.8, 22.7, 14.2, 10.6; HRMS (ESI$^+$): *m/z* calculated for formula $C_{25}H_{27}NNaO_3$ [MNa^+]: 412.1883; found 412.1890; IR (ν_{max}, solid, cm^{-1}): 2959, 2921, 2860, 1759, 1667, 1626, 1601, 1590, 1485, 1472, 1350, 1319, 1282, 1255, 1196, 1099, 1076, 1043.

12-Hexyl-10-(methoxymethoxy)isoindolo[2,1-*b*]isoquinoline-5,7-dione (9c). The desired compound was isolated as a colourless crystalline solid (138 mg, 40%) from methyl 4-(methoxymethoxy)-2-(oct-1-yn-1 yl)benzoate (**10c**) (345 mg, 1.13 mmol) following the general procedure. After 16 hours the reaction was concentrated *in vacuo* and THF (5 mL) was added to dissolve the product and precipitate the CsOAc. The solid was removed by filtration and the filtrate was cooled to 0 °C and acidified with 2N HCl in ether (5.0 mL, 2.5 mmol). After one hour the solid, which had precipitated from the solution, was collected by filtration to afford a cream amorphous solid (138 mg, 35%). A sample was taken and recrystallized from slow diffusion of pentane into a solution of the compound in DMF. Mp 149-151 °C (DMF/pentane); δ_H (500 MHz, $CDCl_3$) 8.56 (1H, d, *J* 7.3), 7.97 (1H, d, *J* 8.5), 7.78-7.72 (2H, m), 7.58 (1H, d, *J* 2.0), 7.54 (1H, ddd, J 8.1, 6.6, 1.7), 7.18 (1H, dd, J 8.4, 2.0), 5.32 (2H, s), 3.54 (3H, s), 3.12-3.06 (2H, m), 1.78-1.71 (2H, m), 1.66-1.58 (2H, m), 1.47-1.34 (4H, m), 0.94 (3H, t, *J* 7.1); δ_C (125 MHz, $CDCl_3$) 164.9, 163.1, 159.8, 137.4, 136.5, 133.9, 130.9, 129.8, 128.6, 128.5, 127.5, 124.0, 122.2, 120.0, 118.4, 110.9, 94.9, 56.6, 31.9, 29.8, 29.3, 26.8, 22.8, 14.2; HRMS (ESI$^+$): *m/z* calculated for formula $C_{24}H_{26}NO_4$ [MH^+]: 392.1856; found 392.1855; IR (ν_{max}, solid, cm^{-1}): 2954, 2922, 2857, 1751, 1669, 1618, 1600, 1479, 1347, 1299, 1274, 1255, 1242, 1229, 1152, 1109, 1076, 1032, 1016.

12-Hexyl-10-hydroxyisoindolo[2,1-*b*]isoquinoline-5,7-dione (9d). 12-Hexyl-10-(methoxymethoxy)isoindolo-[2,1-*b*]-isoquinoline-5,7-dione (**9c**) (140 mg, 0.35 mmol) was dissolved in MeCN (2.5 mL) and cooled to 0 °C. 2 N HCl in ether (5 mL) was added to the reaction mixture, which was stirred overnight. The solvents were removed *in vacuo* and the remaining solid was washed with THF/Et_2O (5 mL) to afford the desired product (76 mg, 62%). A sample was recrystallized from (DMF/pentane)¬¬ to afford colourless crystals. Mp >270 °C (DMF/pentane); δ_H (500 MHz, DMSO-d_6) 10.92 (1H, s), 8.33 (1H, dd, *J* 7.9, 1.3), 7.95 (1H, d, J 8.1), 7.86 (1H, t, *J* 7.6), 7.81 (1H, d, *J* 8.3), 7.62 (1H, t, *J* 7.2), 7.36 (1H, d, *J* 1.8), 7.03 (1H, dd, *J* 8.4, 1.9), 3.11-3.04 (2H, m), 1.68 (4H, m), 1.42-1.29 (4H, m), 0.90 (3H, t, *J* 7.1); δ_C (125 MHz, DMSO-d_6) 164.0, 158.5, 137.0, 136.0, 134.2, 130.5, 128.5, 128.4, 127.7, 127.2, 124.6, 119.0, 118.7, 117.8, 110.1, 31.2, 28.8, 28.7, 25.6, 22.1, 13.9; HRMS (ESI$^+$): *m/z* calculated for formula $C_{22}H_{22}NO_3$ [MH^+]: 348.1594; found 348.1593; IR (ν_{max}, solid, cm^{-1}): 2959, 2924, 2853, 1741, 1667, 1640, 1628, 1592, 1475, 1433, 1416, 1391, 1352, 1322, 1295, 1277, 1262, 1239, 1204, 1153, 1089, 1032, 1010.

3-(2,2-Dimethyl-4-oxo-4*H*-benzo[*d*][1,3]dioxin-5-yl)-4-hexylisoquinolin-1(2*H*)-one (11e). 2,2-Dimethyl-5-(oct-1-yn-1-yl)-4*H*-benzo[*d*][1,3]dioxin-4-one (**10d**) (138 mg, 0.480 mmol) was added to a solution of *N*-(pivaloyloxy)benzamide (**1a**) (110 mg, 0.500 mmol), CsOAc (30 mg, 0.30 mmol) and $[Cp^*RhCl_2]_2$ (3.0 mg, 0.005 ⍰mol) in MeOH (2.5 mL, 0.20 M). After 16 hours consumption of the starting material was observed by TLC. The reaction was concentrated *in vacuo* and purified by flash silica chromatography using 8% isopropanol in toluene to afford an orange-brown solid (195 mg, 96%). The solid was triturated with cold Et_2O (3 × 5 mL) to afford a colourless solid (143 mg, 71%). A sample was taken and recrystallised from $CHCl_3$ and pentane using a vapour diffusion to afford colourless cubic crystals. Mp 231-234 °C ($CHCl_3$/pentane); δ_H (500 MHz, $CDCl_3$) 10.25 (1H, s), 8.27 (1H, d, *J* 8.2), 7.71-7.65 (2H, m), 7.63 (1H, t, *J* 7.5), 7.43 (1H, ddd, *J* 8.1, 5.9, 2.3), 7.15 (1H, dd, J 8.0, 0.7), 7.10 (1H, dd, *J* 7.5, 0.9), 2.51 (1H, ddd, *J* 14.4, 10.0, 6.4), 2.39 (1H, ddd, *J* 14.3, 9.9, 6.6), 1.81 (3H, s), 1.74 (3H, s), 1.53-1.43 (2H, m), 1.25-1.11 (6H, m), 0.82 (3H, t, *J* 7.0); δ_C (125 MHz, $CDCl_3$) 162.8, 158.4, 157.3, 138.2,

137.4, 135.6, 135.5, 132.4, 128.0, 126.0, 123.8, 118.9, 114.0, 113.0, 106.1, 31.6, 29.9, 29.7, 27.9, 26.2, 25.6, 22.7, 14.1, one quaternary carbon was not observed; HRMS (ESI$^+$): *m/z* calculated for formula $C_{25}H_{28}NO_4$ [MH$^+$] 406.2013: found 406.2023; IR (ν_{max}, solid, cm^{-1}): 2952, 2926, 2856, 1742, 1647, 1602, 1583, 1478, 1381, 1311, 1276, 1202, 1044.

12-Hexyl-8-hydroxyisoindolo[2,1-*b*]isoquinoline-5,7-dione (9e). Sodium hydride (100 mg, 2.50 mmol, 60% dispersion in oil) was triturated with petrol (2 × 5 mL) under nitrogen and diluted in THF (10 mL). In a separate flask, 3-(2,2-dimethyl-4-oxo-4H-benzo[d][1,3]-dioxin-5-yl)-4-hexylisoquinolin-1(2H)-one (**11e**) (100 mg, 0.25 mmol) was dissolved in THF (5 mL) and cooled to 0 °C. An aliquot of the sodium hydride solution (1.00 mL, 0.25 mmol) was added dropwise to the reaction. The homogeneous solution changed colour from pale yellow to bright orange, indicating formation of the phenolate ion. An additional aliquot of the sodium hydride solution (1.00 mL, 0.25 mmol) was added in order to achieve full conversion. The reaction mixture was quenched with acetic acid (0.5 mL), at which point the solution changed colour from orange to bright yellow. The reaction was concentrated *in vacuo* and the residue was rediluted in acetic acid (1 mL). The resultant solid was filtered and washed with Et_2O (2 mL) to afford an amorphous yellow solid (55 mg, 63%). The solid was recrystallised from AcOH. Mp 215-218 °C (AcOH); δ_H (500 MHz, $CDCl_3$) 8.69 (1H, s), 8.56 (1H, d, *J* 7.9), 7.77-7.76 (2H, m), 7.63 (1H, t, *J* 8.0), 7.58-7.55 (1H, m), 7.37 (1H, d, *J* 7.7), 7.00 (1H, d, *J* 8.2), 3.14-3.07 (2H, m), 1.77-1.70 (2H, m), 1.59 (2H, q, *J* 7.5), 1.45-1.33 (4H, m), 0.94 (3H, t, *J* 7.0); δ_C (126 MHz, $CDCl_3$) 168.2, 159.7, 158.2, 137.4, 136.5, 135.2, 134.2, 131.0, 129.9, 128.7, 128.1, 124.2, 121.4, 117.2, 115.6, 112.8, 31.8, 29.9, 29.1, 26.9, 22.8, 14.2; HRMS (ESI$^+$): m/z calculated for formula $C_{22}H_{22}NO_3$ [MH$^+$]: 348.1594; found 348.1590; IR (ν_{max}, solid, cm^{-1}): 3220, 2959, 2919, 2854, 1743, 1665, 1612, 1589, 1474, 1458, 1445, 1354, 1341, 1294, 1212, 1189, 1177, 1159, 1117, 1081, 1064, 1038.

3-(2,2-Dimethyl-4-oxo-4*H*-benzo[*d*][1,3]dioxin-5-yl)-4-hexylbenzo[g]isoquinolin-1(2H)-one (11f). 2,2-Dimethyl-5-(oct-1-yn-1-yl)-4*H*-benzo[*d*][1,3]dioxin-4-one **10d** (315 mg, 1.10 mmol) was added to a solution of *N*-(pivaloyloxy)-2-napthamide (**6b)** (271 mg, 1.00 mmol), CsOAc (384 mg, 2.00 mmol) and $[Cp^*RhCl_2]_2$ (6.0 mg, 0.01 mmol) in MeOH (5 mL, 0.2 M). After 2 hours the reaction was concentrated *in vacuo* and a ^{1}H NMR of the crude reaction mixture indicated a mixture of regioisomers. The crude material was purified by flash silica chromatography using 50% EtOAc in pentane to afford an orange-brown solid (231 mg, 51%) and mixed fractions containing a mixture of regioisomers (5:2, 124 mg, 27%). A sample from the pure fractions was removed and crystallised from slow mixing of THF and pentane to afford colourless crystals. Mp 194-197 °C (THF/pentane); δ_H (500 MHz, $CDCl_3$) 9.77 (1H, s), 8.89 (1H, s), 8.12 (1H, s), 8.02 (1H, d, *J* 8.2), 7.97 (1H, d, *J* 8.3), 7.64 (1H, dd, *J* 8.3, 7.6), 7.58 (1H, ddd, *J* 8.2, 6.8, 1.2), 7.51 (1H, ddd, *J* 8.0, 6.8, 1.1), 7.18-7.15 (2H, m), 2.66-2.57 (1H, m), 2.55-2.46 (1H, m), 1.80 (3H, s), 1.75 (3H, s), 1.60-1.52 (2H, m), 1.31-1.15 (6H, m), 0.84 (3H, t, *J* 7.0); δ_C (126 MHz, $CDCl_3$) 163.3, 158.4, 157.3, 137.7, 135.7, 135.6, 134.2, 134.1, 131.3, 129.4, 129.2, 128.1, 126.2, 126.0, 124.7, 122.4, 118.9, 113.7, 113.0, 106.1, 31.6, 29.7, 29.7, 28.2, 26.0, 25.7, 22.7, 14.2; HRMS (ESI$^+$): *m/z* calculated for formula $C_{29}H_{30}NO_4$ [MH$^+$]: 456.2169; found 456.2172; IR (ν_{max}, solid, cm^{-1}): 2927, 2857, 1746, 1737, 1650, 1622, 1597, 1581, 1476, 1442, 1381, 1362, 1314, 1273, 1240, 1200, 1149, 1096, 1040.

14-Hexyl-4-hydroxybenzo[*g*]isoindolo[2,1-*b*]isoquinoline-5,7-dione (9f). Sodium hydride (19 mg, 0.81 mmol, 60% dispersion in oil) was triturated with pentane (2 × 1 mL) under nitrogen and diluted in THF (0.5 mL). In a separate vial, 3-(2,2-dimethyl-4-oxo-4*H*-benzo[*d*][1,3]dioxin-5-yl)-4-hexylbenzo[g]isoquinolin-1(2H)-one (**11f**) (88 mg, 0.19 mmol) was dissolved in THF (3 mL, 0.06 M) and cooled to 0 °C. The sodium hydride solution was added dropwise to the reaction. The homogeneous solution changed colour from pale yellow to bright orange, indicating formation of the phenolate ion. After 30 minutes the reaction was quenched with acetic acid (0.5 mL), at which point the solution changed colour from orange to bright yellow. The reaction mixture was concentrated *in vacuo* and the residue was triturated with water (1 mL) and dissolved into DCM (15 mL),

dried ($MgSO_4$), filtered and concentrated *in vacuo* to afford a yellow amorphous solid (52 mg, 69%). The solid was crystallised by slow evaporation of $CHCl_3$ to afford yellow needles. Mp 244-246 °C ($CHCl_3$); δ_H (500 MHz, $CDCl_3$) 9.04 (1H, s), 8.73 (1H, s), 8.14 (1H, s), 8.00 (1H, d, *J* 8.2), 7.97 (1H, d, *J* 8.3), 7.65-7.61 (2H, m), 7.55 (1H, ddd, *J* 8.0, 6.8, 1.1), 7.38 (1H, d, *J* 7.8), 6.96 (1H, d, *J* 8.3), 3.24-3.17 (2H, m), 1.82-1.76 (2H, m), 1.68-1.61 (2H, m), 1.49-1.35 (4H, m), 0.95 (3H, t, *J* 7.2); δ_C (126 MHz, $CDCl_3$) δ 167.9, 159.9, 157.9, 137.1, 135.9, 135.0, 132.2, 131.7, 130.0, 129.5, 129.3, 128.4, 127.6, 125.0, 124.0, 121.9, 116.7, 115.5, 112.9, 31.7, 29.8, 28.9, 26.9, 22.7, 14.1, missing a quaternary carbon. HRMS (ESI^+): *m/z* calculated for formula $C_{26}H_{23}NNaO_3$ [MNa^+]: 420.1570; found 420.1571; IR (ν_{max}, solid, cm^{-1}): 3243, 2950, 2923, 2873, 2854, 1742, 1664, 1619, 1596, 1567, 1490, 1464, 1440, 1347, 1324, 1308, 1277, 1259, 1232, 1209, 1178, 1164, 1076, 1055, 1015.

2-(5-Bromothiophen-2-yl)-12-hexyl-8-propoxyisoindolo[2,1-b]isoquinoline-5,7-dione (9g). The desired compound was isolated as a dark orange-brown microcrystalline powder (39 mg, 70 mmol, 28%) from methyl 2-(1-octynyl)3-propoxybenzoate (**1c**) (151 mg, 0.50 mmol) following the general procedure. The product was purified by recrystallization from DCM/Et_2O. Mp 202.4-202.7 °C (DCM/Et_2O); δ_H (300 MHz, $CDCl_3$) 8.46 (1H, d, *J* 8.3), 7.73 (1H, d, *J* 1.5), 7.61 (1H, d, *J* 7.9), 7.57 (1H, dd, *J* 1.8, 8.2), 7.54 (1H, d, *J* 7.8), 7.17 (1H, d, *J* 3.9), 7.05 (1H, d, *J* 3.9), 6.92 (1H, d, *J* 8.3), 4.07 (2H, t, *J* 6.5), 3.05 (2H, t, *J* 8.1), 1.93-1.81 (2H, m), 1.67-1.61 (4H, m), 1.38-1.32 (4H, m), 1.06 (3H, t, *J* 7.4), 0.89 (3H, t, *J* 7.0); δ_C (75 MHz, $CDCl_3$) 165.1, 159.1, 144.4, 138.4, 137.2, 136.3, 135.9, 131.6, 131.4, 130.4, 128.5, 127.1, 125.2, 124.9, 120.3, 118.7, 115.5, 113.7, 113.4, 70.6, 31.6, 29.6, 28.8, 26.4, 22.7, 22.4, 14.1, 10.4; HRMS (ESI^+): *m/z* calculated for formula $C_{29}H_{28}{}^{80}BrNNaO3S$ [MNa^+] 572.0866; found 572.0869; IR (ν_{max}, solid, cm^{-1}): 2960, 2921, 2853, 1758, 1670, 1621, 1598, 1588, 1484, 1468, 1328, 1279, 1072, 1168, 1125.

Absorption/emission measurements

UV-Vis absorbance measurements were recorded on a Perkin-Elmer UV/VIS/NIR Spectrometer Lambda 900. Fluorescence measurements were performed using Jobin Yvon Horiba FluoroMax-3 in a 1 cm-pathlength cell without an incident ray filter and the Xenon lamp calibrated to 467 nm and water peak to 397 nm. The excitation and emission slit widths were set to 1 nm. Spectrophotometric grade solvents were purchased from Sigma-Aldrich. Solvents were undegassed during the measurements. 9,10-Diphenylanthracene (97%) was purchased from Sigma-Aldrich and subsequently recrystallised from toluene to afford yellow needles. Solutions for absorbance and fluorescence studies were prepared prior to the experiment and used within 8 hours. The solutions were stored at 0 °C in the dark to prevent photodegradation. The literature value for fluorescence quantum yield for 9,10 diphenylanthracene[32] is specified in cyclohexane (Φ□□□□□□2□, corrected to 0.93 for measurements performed in DCM. Absorbance and fluorescence data for 9,10 diphenylanthracene in DCM and cyclohexane were recorded using solutions prepared from serial dilutions using stock solutions in the corresponding solvent (4.33×10^{-6} M). The emission for 9,10-diphenylanthracene in DCM and cyclohexane (Cy) was integrated from 363-552 nm, with excitation at 375 nm. The quantum yield of fluorescence was determined by comparison of the integrated area of the corrected emission spectrum of the imide **9** to that of 9,10-diphenylanthracene as a standard fluorescence reference. Absorbance and fluorescence data for 9,10 diphenylanthracene and the imides **5** were recorded using solutions in DCM prepared from serial dilutions from stock solutions (standard: 5.19×10^{-6} M; imide: 4.33×10^{-6} M). The emission for 9,10-diphenylanthracene and imides **9** was integrated from 380-545 nm with excitation at 383 nm and 375 nm, respectively.

Cyclic Voltammetry

Electrochemical measurements were conducted using an Autolab PGSTAT20 voltammetric analyser under an argon atmosphere, solvated in pre-dried CH_3CN containing 0.10 M [$^nBu_4N$]BF_4 as supporting electrolyte.

Voltammetric experiments utilised a Pt disk working electrode, a Pt rod auxiliary electrode and an Ag/AgCl reference electrode. All potentials quoted are referenced to an internal ferrocene/ferrocenium standard and were obtained at various scan rates of 10-1000 mVs-1. The ferrocene/ferrocenium couple under these conditions was observed at + 0.45 ≤ $E_{1/2}$ ≤ 0.47 V vs Ag/AgCl.

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Supplementary Material

Details of the preparations of alkynes **10a**-**d**, cyclic voltammograms for **9b**/**9g**, copies of ^{1}H and ^{13}C NMR spectra and crystallographic details for **9a** and **13** are available as Supporting Information.

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