The palladium-catalysed copper-free Sonogashira coupling of isoindoline nitroxides: a convenient route to robust profluorescent carbon–carbon frameworks†

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A series of novel acetylene-substituted isoindoline nitroxides were synthesised *via* palladium-catalysed copper-free Sonogashira coupling. These results demonstrate that the Sonogashira reaction is suitable for the generation of a wide range of aryl nitroxides of expanded structural variety. The novel aryl-iodide containing nitroxide, 5-iodo-1,1,3,3-tetramethylisoindolin-2-yloxyl, **3**, was a key intermediate for this coupling, giving acetylene-substituted isoindoline nitroxides in high yield. Subsequent reaction of the deprotected ethynyl nitroxide **12** with iodinated polyaromatics furnished novel aromatic nitroxides with extended-conjugation. Such nitroxides have been described as profluorescent, as their quantum yields are significantly lower than those of the corresponding diamagnetic derivatives. The quantum yields of the naphthyl- and phenanthryl-acetylene isoindoline nitroxides (**13** and **14**) were found to be ~200-fold and ~65-fold less than the non-radical methoxyamine derivatives (**23** and **24**). Ethyne- and butadiyne-linked nitroxide dimers could also be synthesised by this cross coupling methodology.

Introduction

Aryl-acetylenes are common precursors in the synthesis of natural products, pharmaceuticals and organic molecular materials.[1] Since the initial investigations in 1975 by Cassar,[2] Heck and Dieck,[3] and Sonogashira *et al*.,[4] the Pd-catalysed alkynylation reaction (now often referred to as the Sonogashira reaction) has proven to be a convenient and frequently utilised method for the synthesis of aryl-acetylenes.[5] Whilst aryl-acetylenes are accessible *via* several Pd-catalysed cross coupling methodologies such as Stille (Sn), Suzuki (B) and Negishi (Zn) couplings,[1] the Sonogashira reaction remains attractive because the generation of alkynyl-organometallics is not required prior to the coupling reaction. Rather, with respect to the traditional Sonogashira reaction, a Cu-acetylide is formed *in situ* from a Cu(I) co-catalyst. The use of alkylamines, such as triethylamine, as the solvent is commonplace since these also serve as a base to remove the hydrogen halide (HX) generated from the reaction.[5] The Cu(I) salts commonly used in Sonogashira couplings are also known to catalyse the homocoupling of terminal alkynes in the presence of Pd catalysts.[6–9] These are often observed as unwanted side reactions when coupling to less activated aryl-halides,[10] and copper-free Sonogashira coupling has been employed to address this.[6,10–15] The nature of the amine is critical, as it performs multiple roles in the coupling reaction, including accelerating oxidative insertion and acting as a ligand and a base.[16] Cyclic amines are most commonly employed, as they often lead to enhanced yields in comparison to simple alkylamines.[17]

Although Sonogashira couplings to *t*-butylphenyl,[18,19] nitronyl[19–21] and pyrroline[22] nitroxides have been described, these reactions are often performed on somewhat activated starting materials. To date, little has been reported on Sonogashira reactions using more deactivated aromatic halogenated nitroxides, such as the isoindolines, as coupling partners.

Despite possessing some advantages over commercially available nitroxides, including structural rigidity, superior EPR linewidths[23–26] and enhanced thermal and chemical stability,[27] applications of the isoindoline class of nitroxides have been limited, in part, by a lack of structural variation. Expansion of the structural diversity of the isoindoline nitroxides is particularly important with regards to the generation of extended conjugated systems that possess substantial (masked) fluorescence. These compounds possess interesting fluorescence properties as quenching of the fluorophore excited state, *via* enhanced intersystem crossing, by the unpaired electron of the nitroxide makes these nitroxide–fluorophore hybrids profluorescent.[28,29] Such profluorescent nitroxides are able to detect reactive species by radical scavenging or by redox activity as indicated by an increase in fluorescence generated by the diamagnetic derivatives, such as the alkoxyamine or hydroxylamine.[30–33]

Herein we report the first Sonogashira couplings performed on the isoindoline class of nitroxides. The syntheses of two novel profluorescent acetylene-linked nitroxides incorporating naphthalene and phenanthrene fluorophores are detailed and their fluorescent properties reported. Furthermore, the synthesis of two novel acetylene-linked dinitroxides arising from coupling of the terminal acetylene nitroxide is described.

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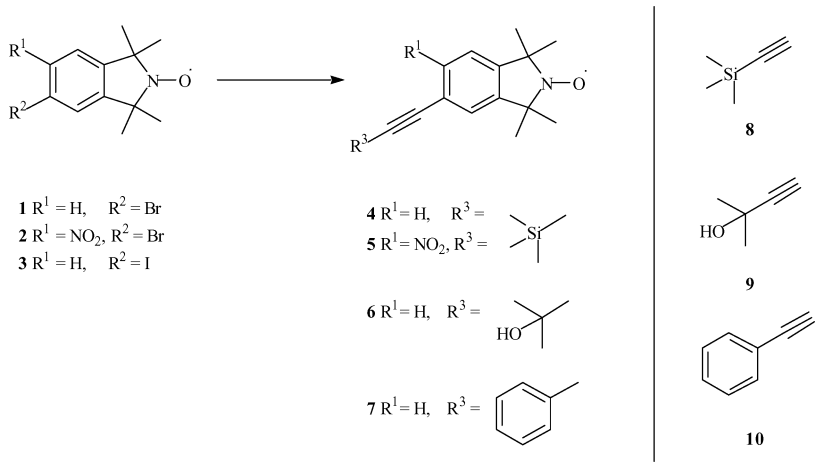
† Electronic supplementary information (ESI) available: Scheme and full details of experimental conditions attempted for the Sonogashira couplings of halogenated isoindoline nitroxides **1–3** and alkynes **8–10**. See DOI: 10.1039/b806963h



Scheme 1 Sonogashira coupling of isoindoline nitroxides.

Results and discussion

Synthesis of novel nitroxides *via* Pd-catalysed Sonogashira coupling

Recently, we have shown that the Pd-catalysed Heck coupling can be successfully performed on brominated isoindoline nitroxides,[34] although more vigorous conditions than commonly employed are required to obtain acceptable yields. With this result in hand, we first attempted Sonogashira couplings with the bromo nitroxide **1** (Scheme 1), using the typical conditions of $Pd(PPh_3)_2Cl_2$–CuI as the catalyst and triethylamine as the solvent/base.[35] None of the targeted products were obtained using these conditions when attempting to couple (trimethylsilyl)acetylene **8** or phenylacetylene **10** to the bromo nitroxide **1** at either room temperature or in refluxing triethylamine (see entries 1–4, Table 1). Instead only starting material **1** and the homocoupled alkynes (butadiynes) could be isolated from the reaction mixture. The presence of CuI is known to disfavour the Sonogashira cross coupling of less active aryl halides,[6] promoting the homocoupling of the acetylene compounds. Nitration of the bromo nitroxide **1**, with HNO_3–H_2SO_4[24] in AcOH gave the nitro-bromo nitroxide **2** in excellent yield (95%). The attempted coupling of (trimethylsilyl)acetylene **8** with the nitro-bromo compound **2**, with presumably reduced electron density, still only yielded the homocoupled acetylenes.

The coupling reactions between (trimethylsilyl)acetylene **8** and the bromo nitroxide **1** or the nitro-bromo nitroxide **2**, utilising the aerobic copper-free conditions of Li *et al*.[6] (2 mol% $Pd(OAc)_2$, 3 equiv. DABCO, MeCN, air, 50 °C) gave trace amounts of both the (trimethylsilyl)acetylene nitroxide **4** and the nitro-(trimethylsilyl)acetylene nitroxide **5**, which were observed by GCMS of the crude reaction mixture. When performed at 80 °C in air, the yields did not increase markedly, whilst under an argon atmosphere at 80 °C the yields could be increased to 5% and 9% for **4** and **5** respectively (see entries 5 and 6, Table 1). Attempts to couple 2-methyl-3-butyn-2-ol **9** and phenylacetylene **10** under the same conditions gave only trace amounts of the desired compounds. Further attempts to optimise the bromo coupling, including increasing the catalyst loadings and using Heck-type conditions did not improve the yield of the reaction. Additional equivalents of (trimethylsilyl)acetylene **8** only improved the reaction slightly (entry 7), whilst an increased reaction temperature, in MeCN or DMF, did not increase the yield of the desired product, with the DMF reactions failing to produce any of the desired product.

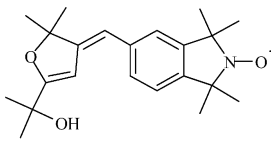
Due to the low reactivity of the brominated isoindoline nitroxides towards palladium-catalysed reactions, a limitation we previously encountered whilst investigating Heck couplings,[34] we investigated the use of the iodo nitroxide[30] **3** to improve the viability of the reaction. Aryl-iodides are known to undergo oxidative

Table 1 Sonogashira couplings of halogenated isoindoline nitroxides and alkynes

Entry	Nitroxide	Alkyne	Catalyst system and solvent	Conditions	Product	Isolated yield (%)
1	**1**	**8** (1.2 equiv.)	$Pd(PPh_3)_2Cl_2$ (2 mol%), CuI (0.5 mol%), Et_3N	rt, Ar, 72 h	**4**	0
2	**1**	**10** (2 equiv.)	$Pd(PPh_3)_2Cl_2$ (2 mol%), CuI (10 mol%), Et_3N	rt, Ar, 96 h	**7**	0
3	**1**	**8** (1.2 equiv.)	$Pd(PPh_3)_2Cl_2$ (2 mol%), CuI (0.5 mol%), Et_3N	90 °C, Ar, 72 h	**4**	0
4	**1**	**10** (2 equiv.)	$Pd(PPh_3)_2Cl_2$ (2 mol%), CuI (10 mol%), Et_3N	90 °C, Ar, 96 h	**7**	0
5	**1**	**8** (5 equiv.)	$Pd(OAc)_2$ (2.5 mol%), DABCO (3 equiv.), MeCN	80 °C, Ar, 72 h	**4**	5
6	**2**	**8** (5 equiv.)	$Pd(OAc)_2$ (2.5 mol%), DABCO (3 equiv.), MeCN	80 °C, Ar, 72 h	**5**	9
7	**1**	**8** (20 equiv.)	$Pd(OAc)_2$ (2.5 mol%), DABCO (3 equiv.), MeCN	80 °C, Ar, 72 h	**4**	8[a]
8	**3**	**8** (5 equiv.)	$Pd(OAc)_2$ (2.5 mol%), DABCO (3 equiv.), MeCN	80 °C, Ar, 24 h	**4**	92
9	**3**	**9** (5 equiv.)	$Pd(OAc)_2$ (2.5 mol%), DABCO (3 equiv.), MeCN	80 °C, Ar, 24 h	**6**	78
10	**3**	**10** (5 equiv.)	$Pd(OAc)_2$ (2.5 mol%), DABCO (3 equiv.), MeCN	80 °C, Ar, 24 h	**7**	96

[a] Yield determined by HPLC, product not isolated.

addition more readily in Pd-catalysed couplings.[36] Indeed, in this case, the coupling of (trimethylsilyl)acetylene **8** with iodo nitroxide **3** (2 mol% $Pd(OAc)_2$, 3 equiv. DABCO, MeCN, argon, 80 °C, 24 h), gave the (trimethylsilyl)acetylene nitroxide **4** in an excellent yield (92%) (see entry 8, Table 1), although the product was difficult to separate from the starting material **3** using standard chromatography. By comparison the bromo nitroxide **1** gave a poor yield of **4** (5%) using the same reaction conditions. Reaction of the iodo nitroxide **3** with 2-methyl-3-butyn-2-ol **9** and phenylacetylene **10** gave the desired acetylene nitroxides **6** and **7**, with yields of 78% and 96% respectively (see entries 9 and 10, Table 1). The reduced yield of the dimethyl propargyl alcohol nitroxide **6** can be attributed to a competing cyclotrimerisation reaction,[37] which gives a substituted 3-benzylidene-2,3-dihydrofurane nitroxide **11** as an undesired side product (detected by GCMS of the reaction mixture).



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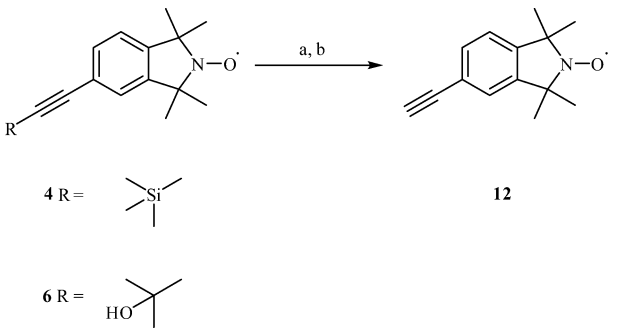
Treatment of the (trimethylsilyl)acetylene nitroxide **4** with aqueous KOH in MeOH gave the desired terminal alkyne nitroxide **12** in 90% yield (see Scheme 2a). Although this method resulted in a high product yield, separation of the desired product **12** from the starting material **4** proved troublesome on a preparative scale due to the loss of band resolution when using greater loadings on the silica gel columns. Thus, an alternative alkyne protecting group was employed for the synthesis of the alkyne nitroxide **12**.

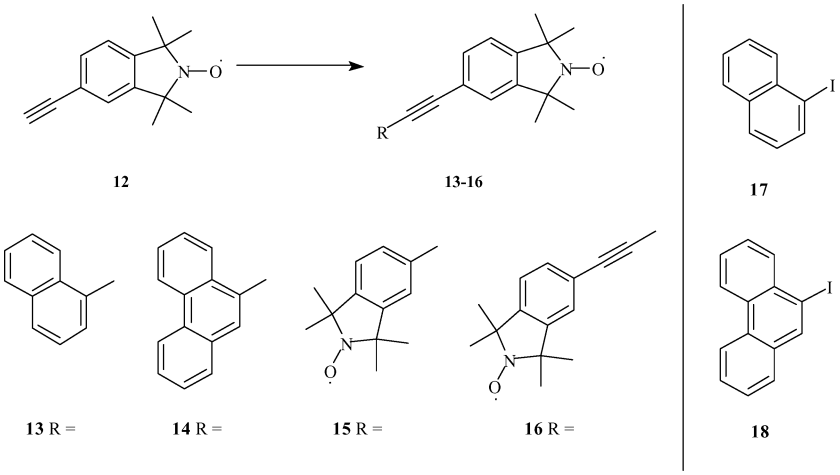
Treatment of the dimethyl propargyl alcohol nitroxide **6** with KOH in refluxing toluene gave the acetylene nitroxide **12** in high yield (88%) (see Scheme 2b). The presence of the polar OH group facilitated the separation of traces of the protected alkyne **6** from the product **12**, which allowed **12** to be isolated in larger quantities and in higher purity than when prepared from the (trimethylsilyl)acetylene nitroxide **4**. Therefore, this was the synthetic route of choice for the synthesis of **12** for use in the subsequent coupling reactions.



Scheme 2 Synthesis of acetylene nitroxide **12**. *Reagents and conditions*: (a) **4**, 0.5 M KOH, MeOH, rt, 1 h (90 %) ; (b) **6**, KOH (8 equiv.), toluene, 110 °C, 1 h (88 %).

The Sonogashira coupling of the acetylene nitroxide **12** with 1-iodonaphthalene **17** (2 mol% $Pd(OAc)_2$, 3 equiv. DABCO, MeCN, Ar, 80 °C, 4 h) gave the naphthylacetylene nitroxide **13** (Scheme 3) in high yield (78%) (see entry 1, Table 2). Due to the electron deficiency of 1-iodonaphthalene **17**, the reaction rate was significantly increased (complete conversion within 4 h) compared with the coupling reactions performed on the iodo nitroxide **3** (*cf*. 24 h). Similar results were obtained using 9-iodophenanthrene **18** as the aryl-halide coupling partner, giving the phenanthrylacetylene nitroxide **14** in 90% yield within 4 h (entry 2, Table 2). Although the homocoupled side product, a butadiyne-linked nitroxide dimer **16**, can be detected by TLC of the reaction mixture, the high reactivity of both aryl halides **17** and **18**, ensured that **16** was only formed in trace amounts and could be readily separated from the desired products.

Coupling of the iodo nitroxide **3** and the acetylene nitroxide **12** gave the targeted acetylene-linked dinitroxide **15**, albeit in a moderate yield of 36% (see entry 3, Table 2). The butadiyne-linked nitroxide dimer **16** was again a side product of the reaction, although due to the decrease in reactivity of the aryl-halide **3** (complete conversion 24 h), it was formed in larger amounts (40%). The formation of the homocoupled product **16**, and the resulting decrease in the concentration of alkyne **12**, may explain the diminished yield of this reaction compared to those using aryl halides **17** and **18**.



Scheme 3 Sonogashira and Eglinton couplings with alkyne nitroxide **12**.

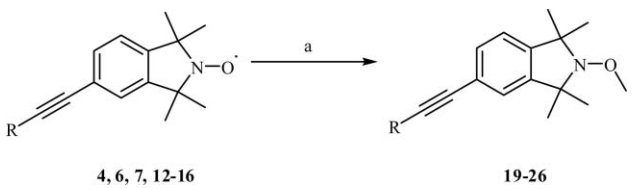
Table 2 Sonogashira and Eglinton couplings of alkyne nitroxide **12**

Entry	Aryl halide	Reagents	Conditions	Product	Isolated yield (%)
1	**17**	$Pd(OAc)_2$ (2.5 mol%), DABCO (3 equiv.), MeCN	80 °C, Ar, 4 h	**13**	78
2	**18**	$Pd(OAc)_2$ (2.5 mol%), DABCO (3 equiv.), MeCN	80 °C, Ar, 4 h	**14**	90
3	**3**	$Pd(OAc)_2$ (2.5 mol%), DABCO (3 equiv.), MeCN	80 °C, Ar, 24 h	**15**	36
4	N/A	$Cu(OAc)_2$ (1.5 equiv.), MeOH, pyridine	reflux, air, 1 h	**16**	91

The butadiyne nitroxide dimer **16**, obtained as a side product in the Sonogashira reaction, could be selectively synthesised *via* Eglinton oxidative coupling. Refluxing the alkyne nitroxide **12** in pyridine–methanol with $Cu(OAc)_2$ (1.5 equiv.) gave the butadiyne-linked nitroxide dimer **16** in excellent yield (91%).

Synthesis of methoxyamines *via* radical trapping

Methoxyamine analogues **19–26** of the acetylene substituted nitroxides **4**, **6**, **7** and **12–16** were prepared following the previously published literature procedure.[34] Reaction of the nitroxides **4**, **6**, **7** and **12–16** with methyl radicals (formed using Fenton chemistry by reaction of $FeSO_4 \cdot 7H_2O$ with H_2O_2 in DMSO) gave the desired methoxyamine adducts in moderate to high yields (31–82%) (see Scheme 4 and Table 3). Unlike the nitroxide precursors, the methoxyamines **19–26** can be analysed by NMR spectroscopy as the paramagnetic centre is no longer present.



Scheme 3 Synthesis of methoxyamines **19–26**. *Reagents and Conditions*: (a) $FeSO_4 \cdot 7H_2O$, H_2O_2, DMSO, rt, 1 h (31–82%).

Fluorescence

A comparison of the fluorescence spectra of naphthyl nitroxide **13** and its methoxyamine derivative **23** (Fig. 1) and phenanthryl nitroxide **14** and its methoxyamine analogue **24** (Fig. 2) reveals a substantial differential in fluorescence intensity. A measure of the fluorescence suppression of the naphthyl and phenanthryl nitroxides **13** and **14** respectively can be attained by comparison of the quantum yields.

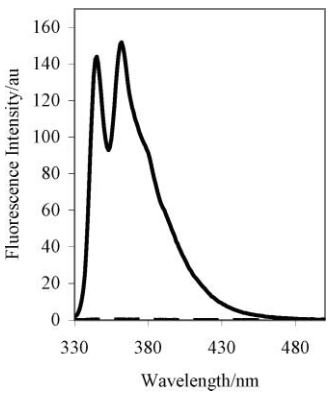
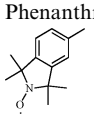
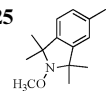
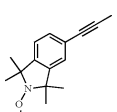
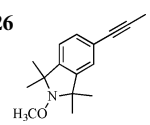


Fig. 1 Fluorescence spectra of **13** (---) and **23** (—) excited at 320 nm in cyclohexane normalised to 1 μM.

Quantum yields of the nitroxides (**13** and **14**) and the methoxyamines (**23** and **24**) were calculated using anthrancene ($\Phi_F = 0.36$, in cyclohexane) as a standard. As expected, the quantum yields of the naphthyl **23** ($\Phi_F = 0.83$) and phenanthryl **24** ($\Phi_F = 0.26$) methoxyamines were significantly larger than the analogous nitroxides **13** ($\Phi_F = 4.0 \times 10^{-3}$) and **14** ($\Phi_F = 4.0 \times 10^{-3}$). The nitroxides **13** and **14** and the phenanthryl methoxyamine **24** have quantum yields similar to related nitroxides and methoxyamines that have been previously reported.[32] Notably,

Table 3 Isolated yields of methoxyamine derivatives of the nitroxides synthesised

Entry	R =	Nitroxide starting material	Methoxyamine product	Isolated yield (%)
1	Me_3Si-	**4**	**19**	79
2	$(CH_3)_2HOC$-	**6**	**20**	55
3	Ph-	**7**	**21**	62
4	H-	**12**	**22**	76
5	Naphthyl-	**13**	**23**	64
6	Phenanthryl-	**14**	**24**	82
7		**15**	**25** 	75
8		**16**	**26** 	31

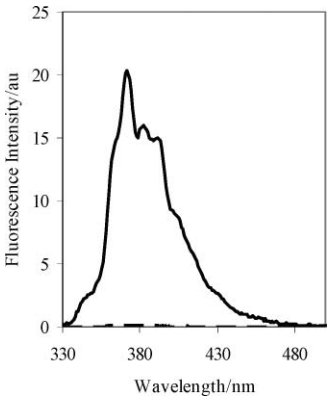
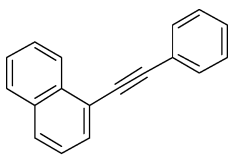


Fig. 2 Fluorescence spectra of **14** (---) and **24** (—) excited at 320 nm in cyclohexane normalised to 1 μM.

the presence of the heterocyclic ring does not impact significantly on the fluorescence quantum yield. To test this we prepared the unsubstituted parent compound 1-(phenylethynyl)naphthalene[14] **27** and recorded its quantum yield. After preparation by coupling 1-iodonaphthalene and phenylacetylene, the quantum yield (Φ_F) of 1-(phenylethynyl)naphthalene **27** in cyclohexane was found to be quite similar (0.80) to the naphthylacetylene methoxyamine **23** (0.83).



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Conclusion

The first examples of palladium-catalysed Sonogashira cross coupling reactions performed on isoindoline nitroxides are reported. Attempts to couple the electron rich bromo nitroxide **1** with substituted alkynes under copper or copper-free Sonogashira conditions were unsuccessful due to the low reactivity of the brominated isoindoline nitroxide **1**. The more reactive iodo nitroxide **3** underwent palladium-catalysed Sonogashira couplings with substituted alkynes under copper-free conditions, to give acetylene nitroxides (**4**, **6** and **7**) in good yield (78–96%). The terminal alkyne nitroxide **12** could be prepared preparatively by cleavage of the 2-methylpropan-2-ol group of **6** with base. Subsequent reaction of the ethynyl nitroxide **12** with iodinated polyaromatics under copper-free Sonogashira conditions gave nitroxides (**13** and **14**) possessing extended conjugation in high yield (78–90%). Notably, the electron deficient nature of the iodinated polyaromatics significantly increased the rate of the reaction compared with use of the iodo nitroxide **3**. Ethyne- and butadiyne-linked dinitroxides (**15** and **16**) could also be formed in moderate yield (36–40%) using this cross coupling approach, but could be raised to 91% using Eglinton conditions. Examination of the fluorescent properties of the profluorescent nitroxides (**13** and **14**) and their corresponding diamagnetic derivatives (**23** and **24**) revealed a significant suppression of fluorescence for the nitroxide containing compounds, which was restored upon formation of the methoxyamines. This Sonogashira cross coupling methodology is currently being investigated for the synthesis of other acetylene extended isoindoline nitroxide systems for a variety of applications. These results will be reported in due course.

Experimental

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance 400 spectrometer in $CDCl_3$. Coupling constants are given in Hz. IR spectra were recorded on a Nicolet 870 Nexus Fourier transform infrared spectrometer equipped with a DTGS TEC detector and an ATR objective. High accuracy mass spectra were recorded using a Micromass autospec double focusing magnetic sector mass spectrometer (EI+ spectra). Formulations were calculated in the elemental analysis programs of Mass Lynx 4.0 or Micromass Opus 3.6. Spectrofluorimetry was performed on a Varian Cary Eclipse fluorescence spectrophotometer equipped with a standard multicell Peltier thermostatted sample holder. All fluorescence measurements were performed in cyclohexane and quantum yields were calculated using anthracene ($\Phi_F = 0.36$) as the standard. Reversed-phase preparatory HPLC was performed on an Agilent 1200 Series prep-HPLC using an Agilent Semi-Prep-C18 (21.2 × 150 mm, 10 μm) column. Melting points were measured on a Gallenkamp variable temperature apparatus by the capillary method. Microanalyses were performed by the Microanalytical Service, Department of Chemistry, University of Queensland. 5-Bromo-1,1,3,3-tetramethylisoindolin-2-yloxyl[38] **1** and 5-iodo-1,1,3,3-tetramethylisoindolin-2-yloxyl[30] **3** were synthesised by the literature procedures.

5-Nitro-6-bromo-1,1,3,3-tetramethylisoindolin-2-yloxyl (2)

To an ice–water cooled solution of 5-bromo-1,1,3,3-tetramethylisoindolin-2-yloxyl **1** (200 mg, 0.74 mmol) in glacial acetic acid (0.6 mL) was added conc. H_2SO_4 (1.15 mL), followed by conc. HNO_3 (0.3 mL). The resultant solution was heated at 40 °C for 4 h, after which the reaction was quenched by the slow addition of NaOH (5 M, 10 mL) and extracted with $CHCl_3$ (3 × 30 mL). The combined organics were washed with water (30 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Recrystallisation from MeCN gave orange needles of 5-nitro-6-bromo-1,1,3,3-tetramethylisoindolin-2-yloxyl **2** (220 mg, 0.70 mmol, 95%); mp 246–248 °C (decomp.); ν_{max} (ATR-FTIR): 3032 (aryl CH), 2979 and 2931 (alkyl CH), 1577 and 1530 (NO_2), 1473 and 1463 (aryl C–C), 1430 ($NO^{\bullet}$) cm^{-1}; +EI MS found M^+ 313.0187 (0.3 ppm from calc. mass of $C_{12}H_{14}BrN_2O_3^{\bullet}$): *m/z* 313 ($M^+$, 63%), 298 (47), 283 (69), 268 (100), 143 (87), 128 (62).

Sonogashira reactions performed using halogenated isoindoline nitroxides (1–3)

The general procedure for the synthesis of substituted acetylene nitroxides **4–7** is given below. The synthesis of the (trimethylsilyl)acetylene nitroxide **4** from the bromo nitroxide **1** is used as a representative example. Alterations of the procedure for the synthesis of **4** using iodo nitroxide **3** as starting material and acetylene nitroxides **5–7** are also given below.

5-[2-(Trimethylsilyl)ethynyl]-1,1,3,3-tetramethylisoindolin-2-yloxyl (4)

5-Iodo-1,1,3,3-tetramethylisoindolin-2-yloxyl **3** (59 mg, 0.186 mmol), 1,4-diazabicyclo[2.2.2]octane (DABCO) (62.5 mg, 0.557 mmol, 3 equiv.) and $Pd(OAc)_2$ (1 mg, 2.5 mol%) were dissolved in dry MeCN (1 mL). (Trimethylsilyl)acetylene **8** (131 μL, 91 mg, 0.927 mmol, 5 equiv.) was added and the mixture heated at 80 °C under argon in a sealed Schlenk vessel for 24 h. The solvent was removed under reduced pressure and the residue taken up in $CHCl_3$ (~1 mL). Purification of the resulting solution by column chromatography (SiO_2, eluant: 10% EtOAc, 90% *n*-hexane) gave 5-[2-(trimethylsilyl)ethynyl]-1,1,3,3-tetramethylisoindolin-2-yloxyl **4** as a yellow–orange gum (49 mg, 0.171 mmol, 92%); (found: C, 70.7; H, 8.5; N, 4.7; $C_{17}H_{24}SiNO^{\bullet}$ requires C, 71.3; H, 8.4; N, 4.9%); ν_{max} (ATR-FTIR): 2972 and 2928 (alkyl CH), 2154 (C≡C), 1487 and 1465 (aryl C–C), 1431 ($NO^{\bullet}$) cm^{-1}; +EI MS found M^+ 286.16265 (0.25 ppm from calc. mass of $C_{17}H_{24}SiNO^{\bullet}$): *m/z* 286 ($M^+$, 12%), 271 (21), 256 (100), 241 (79), 225 (32).

Alternate synthesis of 5-[2-(trimethylsilyl)ethynyl]-1,1,3,3-tetramethylisoindolin-2-yloxyl (4)

5-Bromo-1,1,3,3-tetramethylisoindolin-2-yloxyl **1** (50 mg, 0.186 mmol), DABCO (62.5 mg, 0.557 mmol, 3 equiv.), $Pd(OAc)_2$ (1 mg, 2.5 mol%), (trimethylsilyl)acetylene **8** (131 μL, 91 mg, 0.927 mmol, 5 equiv.) and MeCN (1 mL) were treated as described above. Column chromatography (SiO_2, eluant: 10% EtOAc, 90% *n*-hexane) gave 5-[2-(trimethylsilyl)ethynyl]-1,1,3,3-tetramethylisoindolin-2-yloxyl **4** (3 mg, 0.010 mmol, 5%). GCMS analysis showed that the product was identical to that reported above.

5-[2-(Trimethylsilyl)ethynyl]-6-nitro-1,1,3,3-tetramethylisoindolin-2-yloxyl (5)

5-Nitro-6-bromo-1,1,3,3-tetramethylisoindolin-2-yloxyl **2** (58 mg, 0.186 mmol), DABCO (62.5 mg, 0.557 mmol, 3 equiv.), $Pd(OAc)_2$ (1 mg, 2.5 mol%), (trimethylsilyl)acetylene **8** (131 μL, 91 mg, 0.927 mmol, 5 equiv.) and MeCN (1 mL) were treated as described above. Column chromatography (SiO_2, eluant: 10% EtOAc, 90% *n*-hexane) gave 5-[2-(trimethylsilyl)ethynyl]-6-nitro-1,1,3,3-tetramethylisoindolin-2-yloxyl **5** as a yellow–orange solid (5 mg, 0.016 mmol, 9%); mp 144–147 °C; ν_{max} (ATR-FTIR): 3045 (aryl CH), 2972 and 2927 (alkyl CH), 2150 (C≡C), 1573 and 1523 (NO_2), 1480 and 1467 (aryl C–C), 1431 ($NO^{\bullet}$) cm^{-1}; +EI MS found M^+ 331.14808 (0.85 ppm from calc. mass of $C_{17}H_{23}SiN_2O_3^{\bullet}$): *m/z* 331 ($M^+$, 100%), 316 (43), 301 (52), 286 (22).

5-(3-Hydroxy-3-methyl)butynyl-1,1,3,3-tetramethylisoindolin-2-yloxyl (6)

5-Iodo-1,1,3,3-tetramethylisoindolin-2-yloxyl **3** (1.18 g, 3.73 mmol), DABCO (1.25 g, 11.14 mmol, 3 equiv.), $Pd(OAc)_2$ (20 mg, 2.5 mol%), 2-methyl-3-butyn-2-ol **9** (1.82 mL, 1.60 g, 19 mmol, 5 equiv.) and MeCN (20 mL) were treated as described above. Column chromatography (SiO_2, eluant: 50% EtOAc, 50% *n*-hexane) gave 5-(3-hydroxy-3-methyl)butynyl-1,1,3,3-tetramethylisoindolin-2-yloxyl **6** as a brown–orange oil (797 mg, 2.93 mmol, 78%); (found: C, 74.3; H, 8.3; N, 5.0; $C_{17}H_{22}NO_2^{\bullet}$ requires C, 75.0; H, 8.1; N, 5.1%); ν_{max} (ATR-FTIR): 3387 (OH), 2976 and 2930 (alkyl CH), 2165 (C≡C), 1490 and 1453 (aryl C–C), 1431 ($NO^{\bullet}$) cm^{-1}; +EI MS found M^+ 272.1654 (1.3 ppm from calc. mass of $C_{17}H_{22}NO_2^{\bullet}$): *m/z* 272 ($M^+$, 100%), 257 (95), 242 (92), 227 (87).

5-[2-(Phenyl)ethynyl]-1,1,3,3-tetramethylisoindolin-2-yloxyl (7)

5-Iodo-1,1,3,3-tetramethylisoindolin-2-yloxyl **3** (59 mg, 0.186 mmol), DABCO (62.5 mg, 0.557 mmol, 3 equiv.), $Pd(OAc)_2$ (1 mg, 2.5 mol%), phenylacetylene **10** (102 μL, 95 mg, 0.930 mmol, 5 equiv.) and MeCN (1 mL) were treated as described above. Column chromatography (SiO_2, eluant: 10% EtOAc, 90% *n*-hexane) gave 5-[2-(phenyl)ethynyl]-1,1,3,3-tetramethylisoindolin-2-yloxyl **7** as a yellow–orange solid (52 mg, 0.179 mmol, 96%); mp 108–112 °C; (found: C, 82.0; H, 6.9; N, 4.7; $C_{20}H_{20}NO^{\bullet}$ requires C, 82.7; H, 6.9; N, 4.8%); ν_{max} (ATR-FTIR): 3047 (aryl CH) 2977 and 2928 (alkyl CH), 2214 (C≡C), 1487 and 1465 (aryl C–C), 1431 ($NO^{\bullet}$) cm^{-1}; +EI MS found M^+ 290.1542 (1.0 ppm from calc. mass of $C_{20}H_{20}NO^{\bullet}$): *m/z* 290 (M^+, 90%), 275 (75), 260 (100), 245 (50), 215 (40).

5-Ethynyl-1,1,3,3-tetramethylisoindolin-2-yloxyl (12)

5-(3-Hydroxy-3-methyl)butynyl-1,1,3,3-tetramethylisoindolin-2-yloxyl **6** (478 mg, 1.76 mmol) was dissolved in dry toluene (320 mL). Solid KOH was added (0.8 g, 14.3 mmol, 8 equiv.) and the mixture refluxed for 1 h. The dark brown suspension was washed with water (3 × 200 mL) and brine (200 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. The residue was taken up in $CHCl_3$ (~5 mL) and purified by column chromatography (SiO_2, eluant: 30% EtOAc, 70% *n*-hexane) to give 5-ethynyl-1,1,3,3-tetramethylisoindolin-2-yloxyl **12** as a pale yellow crystalline solid (331 mg, 1.54 mmol, 88%); mp 126–128 °C; ν_{max} (ATR-FTIR): 3196 (≡CH), 2978 and 2929 (alkyl CH), 2097 (C≡C), 1487 and 1464 (aryl C–C), 1428 ($NO^{\bullet}$) cm^{-1}; +EI MS found M^+ 214.1235 (1.5 ppm from calc. mass of $C_{14}H_{16}NO^{\bullet}$): *m/z* 214 (M^+, 86%), 199 (90), 184 (100), 169 (84), 152 (53).

Alternate synthesis of 5-ethynyl-1,1,3,3-tetramethylisoindolin-2-yloxyl (12)

A solution of 5-[2-(trimethylsilyl)ethynyl]-1,1,3,3-tetramethylisoindolin-2-yloxyl **4** (113 mg, 0.39 mmol) was dissolved in degassed MeOH (2.1 mL). Aqueous KOH was added (50 μL, 0.5 M) and the solution was stirred at room temperature for 1 h. The reaction mixture was treated with water (50 mL), extracted with Et_2O (2 × 50 mL), dried (Na_2SO_4) and the solvent was removed under reduced pressure to give the 5-ethynyl-1,1,3,3-tetramethylisoindolin-2-yloxyl **12** and a trace amount of unreacted starting material **4**, which were inseparable by SiO_2 column chromatography. Reversed-phase prep-HPLC (50% THF, 50% H_2O) gave 5-ethynyl-1,1,3,3-tetramethylisoindolin-2-yloxyl **12** as a yellow crystalline solid (78 mg, 0.37 mmol, 90%). GCMS analysis and mp comparison showed that the product was identical to that reported above.

Sonogashira reactions performed using ethynyl nitroxide (12)

The procedure for the synthesis of substituted acetylene nitroxides **13–15** is detailed below. The synthesis of the naphthyl-acetylene nitroxide **13** is used as an example. Alterations of the procedure for the synthesis of acetylene nitroxides **14** and **15** are also described below.

5-[2-(1-Naphthyl)ethynyl]-1,1,3,3-tetramethylisoindolin-2-yloxyl (13)

1-Iodonaphthalene **17** (28.3 μL, 49 mg, 0.193 mmol), DABCO (62.5 mg, 0.557 mmol, 3 equiv.) and $Pd(OAc)_2$ (1 mg, 2.5 mol%) were dissolved in dry MeCN (1 mL). 5-Ethynyl-1,1,3,3-tetramethylisoindolin-2-yloxyl **12** (50 mg, 0.233 mmol, 1.2 equiv.) was added and the mixture heated at 80 °C under argon for 4 h. The solvent was removed under reduced pressure and the residue taken up in $CHCl_3$ (~1 mL). Purification of the resulting solution by column chromatography (SiO_2, eluant: 10% EtOAc, 90% *n*-hexane) gave 5-[2-(1-naphthyl)ethynyl]-1,1,3,3-tetramethylisoindolin-2-yloxyl **13** as an orange solid (51 mg, 0.151 mmol, 78%); mp 145–148 °C; ν_{max} (ATR-FTIR): 3055 (aryl CH), 2972 and 2924 (alkyl CH), 2211 (C≡C), 1488 and 1460 (aryl C–C), 1430 ($NO^{\bullet}$) cm^{-1}; +EI MS found M^+ 340.1701 (0.1 ppm from calc. mass of $C_{24}H_{22}NO^{\bullet}$): *m/z* 340 (M^+, 84%), 325 (60), 310 (100), 295 (32), 265 (35).

5-[2-(9-Phenanthryl)ethynyl]-1,1,3,3-tetramethylisoindolin-2-yloxyl (14)

9-Iodophenanthrene **18** (59 mg, 0.194 mmol), DABCO (62.5 mg, 0.557 mmol, 3 equiv.), $Pd(OAc)_2$ (1 mg, 2.5 mol%), 5-ethynyl-1,1,3,3-tetramethylisoindolin-2-yloxyl **12** (50 mg, 0.233 mmol, 1.2 equiv.) and MeCN (1 mL) were treated as described above. Column chromatography (SiO_2, eluant: 10% EtOAc, 90% *n*-hexane) gave 5-[2-(9-phenanthryl)ethynyl]-1,1,3,3-tetramethylisoindolin-2-yloxyl **14** as an orange solid (52 mg, 0.179 mmol, 90%); mp 175–178 °C; ν_{max} (ATR-FTIR): 3070 (aryl CH), 2971 and 2924 (alkyl CH), 2214 (C≡C), 1490 and 1451 (aryl C–C), 1430 ($NO^{\bullet}$) cm^{-1}; +EI MS found M^+ 390.1857 (0.2 ppm from calc. mass of $C_{28}H_{24}NO^{\bullet}$): *m/z* 390 (M^+, 72%), 375 (45), 360 (100), 345 (25).

1,2-Bis-[5,5′-(1,1,3,3-tetramethylisoindolin-2-yloxylyl)]ethyne (15)

5-Iodo-1,1,3,3-tetramethylisoindolin-2-yloxyl **3** (61 mg, 0.193 mmol), DABCO (62.5 mg, 0.557 mmol, 3 equiv.), $Pd(OAc)_2$ (1 mg, 2.5 mol%), 5-ethynyl-1,1,3,3-tetramethylisoindolin-2-yloxyl **12** (50 mg, 0.233 mmol, 1.2 equiv.) and MeCN (1 mL) were treated as described above and heated at 80 °C for 24 h. Column chromatography (SiO_2, eluant: 10% EtOAc, 90% *n*-hexane) gave the desired 1,2-bis-[5,5′-(1,1,3,3-tetramethylisoindolin-2-yloxylyl)]ethyne **15** and the homocoupled acetylene 1,4-bis-[5,5′-(1,1,3,3-tetramethylisoindolin-2-yloxylyl)]-1,3-butadiyne **16**. Reversed-phase prep-HPLC (45% THF, 55% H_2O) gave 1,2-bis-[5,5′-(1,1,3,3-tetramethylisoindolin-2-yloxylyl)]ethyne **15** as a yellow crystalline solid (28 mg, 0.070 mmol, 36%); mp 214–216 °C (decomp.); ν_{max} (ATR-FTIR): 3045 (aryl CH), 2972 and 2928 (alkyl CH), 2207 (C≡C), 1496 and 1466 (aryl C–C), 1433 ($NO^{\bullet}$) cm^{-1}; +EI MS found M^+ 402.2306 (0.3 ppm from calc. mass of $C_{26}H_{30}N_2O_2^{\bullet\bullet}$): *m/z* 402 ($M^+$, 95%), 387 (40), 372 (50), 357 (100), 342 (83).

1,4-Bis-[5,5′-(1,1,3,3-tetramethylisoindolin-2-yloxylyl)]-1,3-butadiyne (16)

5-Ethynyl-1,1,3,3-tetramethylisoindolin-2-yloxyl **12** (50 mg, 0.233 mmol) and $Cu(OAc)_2$ (65 mg, 0.358 mmol, 1.5 equiv.), were dissolved in MeOH (0.5 mL) and pyridine (0.5 mL) and the resultant mixture was refluxed for 1 h. H_2SO_4 (conc.) was added to the resultant mixture until a suspension formed, which was subsequently extracted with DCM (3 × 20 mL), washed with H_2O (20 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure to give 1,4-bis-[5,5′-(1,1,3,3-tetramethylisoindolin-2-yloxylyl)]-1,3-butadiyne **16** as an orange crystalline solid (45 mg, 0.105 mmol, 91%); mp 183–185 °C (decomp.); ν_{max} (ATR-FTIR): 3046 (aryl CH), 2975 and 2928 (alkyl CH), 2150 (C≡C), 1487 and 1463 (aryl C–C), 1430 ($NO^{\bullet}$) cm^{-1}; +EI MS found M^+ 426.2307 (0.1 ppm from calc. mass of $C_{28}H_{30}N_2O_2^{\bullet\bullet}$): *m/z* 426 ($M^+$, 40%), 411 (28), 396 (35), 381 (100), 366 (33).

Synthesis of methoxyamines (19–24)

A general procedure for the synthesis of methoxyamines **19–24** is shown below. For the synthesis of dimethoxyamines **25** and **26** the amounts of all reagents were doubled.

General procedure

To a solution of acetylene-substituted nitroxide (0.077 mmol) and $FeSO_4 \cdot 7H_2O$ (0.154 mmol, 2 equiv.) in DMSO (2.6 mL) was added H_2O_2 (30%, 18 μL). The reaction mixture was stirred under argon at room temperature for 1.5 h. NaOH (1 M) was added and the resulting solution extracted with Et_2O. The organic phase was washed with H_2O and dried (Na_2SO_4). Removal of the solvent under reduced pressure gave the crude methoxyamine. Subsequent purification was achieved by column chromatography (see below for specific conditions).

5-[2-(Trimethylsilyl)ethynyl]-2-methoxy-1,1,3,3-tetramethylisoindoline (19)

Yield: 18 mg, 0.061 mmol, 79%; chromatography: SiO_2, 10% EtOAc, 90% *n*-hexane; δ_H: 0.27 (9H, s, $SiCH_3$) 1.43 (12H, br s, CH_3), 3.79 (3H, s, $NOCH_3$), 7.04 (1H, dd, *J* 0.5 and 7.8 Hz, 7-H), 7.22 (1H, dd, *J* 0.5 and 1.4 Hz, 4-H), 7.36 (1H, dd, *J* 1.4 and 7.8 Hz, 6-H); δ_C: 0.0 ($SiCH_3$) 30.3 (CH_3), 65.5 (OCH_3), 67.0 (alkyl C*), 67.1 (alkyl C*), 93.3 (C≡C), 105.4 (C≡C), 121.5 (C-7), 121.8 (C-5), 125.2 (C-6), 131.2 (C-4), 145.3 (C-3a), 145.9 (C-7a).

5-(3-Hydroxy-3-methyl)butynyl-2-methoxy-1,1,3,3-tetramethylisoindoline (20)

Yield: 12 mg, 0.042 mmol, 55%; chromatography: SiO_2, 30% EtOAc, 70% *n*-hexane; δ_H: 1.43 (12H, br s, CH_3), 1.64 (6H, s, $\equiv CCCH_3$), 2.06 (1H br s, OH), 3.79 (3H, s, $NOCH_3$), 7.04 (1H, dd, *J* 0.6 and 7.8 Hz, 7-H), 7.18 (1H, dd, *J* 0.6 and 1.5 Hz, 4-H), 7.30 (1H, dd, *J* 1.5 and 7.8 Hz, 6-H); δ_C: 29.7 (CH_3), 31.5 ($\equiv CCCH_3$), 65.5 (≡CC*) 65.7 (OCH_3), 67.0 (alkyl C*), 67.1 (alkyl C*), 82.4 (C≡C), 93.1 (C≡C), 121.4 (C-5), 121.5 (C-7), 124.9 (C-6), 130.8 (C-4), 145.4 (C-3a), 145.6 (C-7a).

5-[2-(Phenyl)ethynyl]-2-methoxy-1,1,3,3-tetramethylisoindoline (21)

Yield: 15 mg, 0.048 mmol, 62%; chromatography: SiO_2, 10% EtOAc, 90% *n*-hexane; δ_H: 1.46 (12H, br s, CH_3), 3.81 (3H, s, $NOCH_3$), 7.10 (1H, d, *J* 7.8 Hz, 7-H), 7.30 (1H, d, *J* 1.5 Hz, 4-H), 7.36 (3H, m, ArH), 7.43 (1H, dd, *J* 1.5 and 7.8 Hz, 6-H), 7.55 (2H, m, ArH); δ_C: 30.3 (CH_3), 65.5 (OCH_3), 67.1 (alkyl C*), 67.2 (alkyl C*), 88.7 (C≡C), 89.7 (C≡C), 121.6 (C-7), 122.0 (C-5), 123.4 (ArC-C≡), 124.8 (C-6), 128.2 (ArC), 128.4 (ArC), 130.8 (C-4), 131.6 (ArC), 145.5 (C-3a), 145.6 (C-7a).

5-Ethynyl-2-methoxy-1,1,3,3-tetramethylisoindolin-2-yloxyl (22)

Yield: 14 mg, 0.059 mmol, 76%; chromatography: SiO_2, 10% EtOAc, 90% *n*-hexane; δ_H: 1.45 (12H, br s, CH_3), 3.07 (1H, s, ≡CH), 3.80 (3H, s, $NOCH_3$), 7.08 (1H, dd, *J* 0.5 and 7.8 Hz, 7-H), 7.27 (1H, dd, *J* 0.5 and 1.4 Hz, 4-H), 7.40 (1H, dd, *J* 1.4 and 7.8 Hz, 6-H); δ_C: 30.3 (CH_3), 65.4 (OCH_3), 66.9 (alkyl C*), 67.1 (alkyl C*), 76.5 (C≡C), 83.9 (C≡C), 120.8 (C-5), 121.5 (C-7), 125.3 (C-6), 131.3 (C-4), 145.5 (C-3a), 146.2 (C-7a).

5-[2-(1-Naphthyl)ethynyl]-2-methoxy-1,1,3,3-tetramethylisoindoline (23)

Yield: 17 mg, 0.049 mmol, 64%; chromatography: SiO_2, 10% EtOAc, 90% *n*-hexane; δ_H: 1.49 (12H, br s, CH_3), 3.82 (3H, s, $NOCH_3$), 7.15 (1H, dd, *J* 0.5 and 7.8 Hz, 7-H), 7.40 (1H, dd, *J* 0.5 and 1.5 Hz, 4-H), 7.48 (1H, m, ArH), 7.56 (2H, m, ArH), 7.63 (1H, m, ArH), 7.78 (1H, dd, *J* 1.5 and 7.8 Hz, 6-H), 7.86 (1H, m, ArH), 7.89 (1H, m, ArH), 8.46 (1H, m ArH); δ_C: 30.3 (CH_3), 65.5 (OCH_3), 67.2 (alkyl C*), 67.3 (alkyl C*), 86.9 (C≡C), 94.6 (C≡C), 121.0 (C-5), 121.7 (C-7), 122.2 (ArC-C≡), 124.8 (C-6), 125.3 (ArC), 126.3 (ArC), 126.4 (ArC), 126.8 (ArC), 128.3 (ArC), 128.7 (ArC), 130.3 (ArC), 130.9 (C-4), 133.2 (ArC), 133.3 (ArC), 145.6 (C-3a), 145.8 (C-7a).

5-[2-(9-Phenanthryl)ethynyl]-2-methoxy-1,1,3,3-tetramethylisoindoline (24)

Yield: 26 mg, 0.063 mmol, 82%; chromatography: SiO_2, 10% EtOAc, 90% *n*-hexane; δ_H: 1.51 (12H, br s, CH_3), 3.83 (3H, s, $NOCH_3$), 7.17 (1H, dd, *J* 0.6 and 7.8 Hz, 7-H), 7.44 (1H, dd, *J* 0.6 and 1.5 Hz, 4-H), 7.59 (1H, dd, *J* 1.5 and 7.8 Hz, ArH), 7.63 (1H, m, ArH), 7.70 (1H, m, ArH), 7.74 (2H, m, ArH), 7.90 (1H, dd, *J* 1.5 and 7.8 Hz, 6-H), 8.11 (1H, s, ArH), 8.58 (1H, m, ArH), 8.70 (1H, m, ArH), 8.74 (1H, m, ArH); δ_C: 30.3 (CH_3), 65.5 (OCH_3), 67.1 (alkyl C*), 67.2 (alkyl C*), 87.1 (C≡C), 94.3 (C≡C), 119.7 (C-5), 121.8 (C-7), 122.1 (ArC-C≡), 122.7 (ArC), 122.8 (ArC), 124.9 (C-6), 125.6 (ArC), 127.0 (ArC), 127.1 (ArC), 127.4 (ArC), 128.6 (ArC), 130.1 (ArC), 130.3 (ArC), 131.0 (C-4), 131.2 (ArC), 131.3 (ArC), 131.8 (ArC), 135.8 (ArC), 145.6 (C-3a), 145.9 (C-7a).

1,2-Bis-[5,5′-(2-methoxy-1,1,3,3-tetramethylisoindoline)]ethyne (25)

Yield: 25 mg, 0.058 mmol, 75%; chromatography: SiO_2, 10% EtOAc, 90% *n*-hexane; δ_H: 1.46 (24H, br s, CH_3), 3.80 (6H, s, $NOCH_3$), 7.09 (2H, dd, *J* 0.6 and 7.8 Hz, 7-H), 7.29 (2H, dd, *J* 0.6 and 1.5 Hz, 4-H), 7.42 (2H, dd, *J* 1.5 and 7.8 Hz, 6-H); δ_C: 30.3 (CH_3), 65.5 (OCH_3), 67.1 (alkyl C*), 67.2 (alkyl C*), 89.0 (C≡C), 121.6 (C-5 and C-5′), 122.1 (C-7 and C-7′), 124.8 (C-6 and C-6′), 130.8 (C-4 and C-4′), 145.4 (C-3a and C-3a′), 145.5 (C-7a and C-7a′).

1,4-Bis-[5,5′-(2-methoxy-1,1,3,3-tetramethylisoindoline)]-1,3-butadiyne (26)

Yield: 11 mg, 0.024 mmol, 31%; chromatography: SiO_2, 10% EtOAc, 90% *n*-hexane; δ_H: 1.45 (24H, br s, CH_3), 3.79 (6H, s, $NOCH_3$), 7.08 (2H, dd, *J* 0.5 and 7.8 Hz, 7-H), 7.28 (2H, dd, *J* 0.5 and 1.5 Hz, 4-H), 7.41 (2H, dd, *J* 1.5 and 7.8 Hz, 6-H); δ_C: 30.3 (CH_3), 65.5 (OCH_3), 67.0 (alkyl C*), 67.2 (alkyl C*), 73.4 (C≡C), 81.8 (C≡C), 120.6 (C-5 and C-5′), 121.8 (C-7 and C-7′), 125.8 (C-6 and C-6′), 131.7 (C-4 and C-4′), 145.6 (C-3a and C-3a′), 146.7 (C-7a and C-7a′).

1-(Phenylethynyl)naphthalene (27)[14]

1-Iodonaphthalene **17** (57.6 μL, 100 mg, 0.393 mmol), DABCO (130 mg, 1.200 mmol, 3 equiv.) and $Pd(OAc)_2$ (2 mg, 2.5 mol%) was dissolved in dry MeCN (1 mL). Phenylacetylene **10** (51.6 μL, 48 mg, 0.470 mmol, 1.2 equiv.) was added and the mixture heated at 80 °C under argon for 4 h. The solvent was removed under reduced pressure and the residue taken up in $CHCl_3$ (~1 mL). Purification of the resulting solution by column chromatography (SiO_2, eluant: 10% EtOAc, 90% *n*-hexane) gave 1-(phenylethynyl)naphthalene **27** as a colourless oil (85 mg, 0.373 mmol, 95%); δ_H: 7.40–7.73 (8H, m ArH), 7.80–7.92 (3H, m, ArH), 8.49–8.53 (1H, m, ArH); δ_C: 87.6 (C≡C), 94.4 (C≡C), 121.0 (ArC), 123.5 (ArC), 125.4 (ArC), 126.3 (ArC), 126.5 (ArC), 126.9 (ArC), 128.4 (ArC), 128.5 (ArC), 128.5 (ArC), 128.9 (ArC), 130.5 (ArC), 131.8 (ArC), 133.3 (ArC), 133.3 (ArC). The NMR data was in agreement with that previously reported.[14]

Fluorescence quantum yield calculations

Fluorescence quantum yield measurements were calculated using cyclohexane as the solvent and anthracene ($\Phi_F = 0.36$) as the standard. Stock solutions of naphthyl and phenanthryl compounds **13**, **14**, **23**, **24** and **27** (approximately 1 mg 100 mL^{-1}, measured accurately, exact concentrations listed below) were diluted using analytical glassware to give four solutions of decreasing concentration, ensuring that the UV–vis absorbance of the highest concentration did not exceed 0.1 absorbance units at the fluorescence excitation wavelength (320 nm). The fluorescence detector voltage was set at 480 V for naphthalenes **13**, **23** and **27** and 600 V for the phenanthrenes **14** and **24**. The total fluorescence emission was plotted against UV–vis absorbance to give a straight line with gradient (m), which was ratioed against the anthracene standard, giving the quantum yield (Φ_F).

Anthracene (28)

Stock solution **28** (1.07 mg, 0.00600 mmol, 0.0600 mM). Diluted to give solutions of 12.000, 9.600, 7.200 and 4.800 μM; $m = 157765$.

5-[2-(1-Naphthyl)ethynyl]-1,1,3,3-tetramethylisoindolin-2-yloxyl (13)

Stock solution **13** (1.07 mg, 0.00314 mmol, 0.0314 mM). Diluted to give solutions of 5.024, 3.768, 2.512 and 1.256 μM; $m = 1896$; $\Phi_F = 0.36\ (1896/157765) = 0.004$.

5-[2-(9-Phenanthryl)ethynyl]-1,1,3,3-tetramethylisoindolin-2-yloxyl (14)

Stock solution **14** (0.99 mg, 0.00254 mmol, 0.0254 mM). Diluted to give solutions of 3.048, 2.540, 2.032 and 1.016 μM; $m = 5514$; $\Phi_F = 0.36\ (5514/1338220) = 0.004$.

5-[2-(1-Naphthyl)ethynyl]-2-methoxy-1,1,3,3-tetramethylisoindoline (23)

Stock solution **23** (1.07 mg, 0.00301 mmol, 0.0301 mM). Diluted to give solutions of 4.816, 3.612, 2.408 and 1.204 μM; $m = 361630$; $\Phi_F = 0.36\ (361630/157765) = 0.825$.

5-[2-(9-Phenanthryl)ethynyl]-2-methoxy-1,1,3,3-tetramethylisoindoline (24)

Stock solution **24** (1.17 mg, 0.00289 mmol, 0.0289 mM). Diluted to give solutions of 4.624, 3.468, 2.312 and 1.156 μM; $m = 40375$; $\Phi_F = 0.36\ (343353/1338220) = 0.257$.

1-(Phenylethynyl)naphthalene (27)[14]

Stock solution **27** (1.08 mg, 0.00473 mmol, 0.0473 mM). Diluted to give solutions of 3.784, 2.838, 1.892 and 0.946 μM; $m = 348354$; $\Phi_F = 0.36\ (348354/157765) = 0.795$.

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