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Tetrahedron 60 (2004) 10983–10992

Stepwise and one-pot cross-coupling–heteroannulation approaches toward 2-substituted C5-, C6-, and C7-nitroindoles☆

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Received 22 June 2004; revised 25 August 2004; accepted 1 September 2004

Available online 30 September 2004

Abstract—A general and efficient synthesis of 2-substituted C5-, C6-, and C7-nitroindoles has been established. Starting from commercially available 2-amino nitrophenols, C5-, C6-, and C7-nitroindoles were synthesized via the stepwise Pd-catalyzed cross-coupling of nitro 2-trifloxyanilides with 1-alkynes followed by the *t*-BuOK-mediated heteroannulation. A Pd-catalyzed one-pot coupling–heteroannulation procedure was carried out by using nitro 2-trifluoroacetamidoaryl triflates.

1. Introduction

Nitroindoles are known to be biologically active[1] and serve as the useful precursors to a variety of nitrogen-substituted indole derivatives, which exhibit diverse regulatory activities on bio-macromolecules. Selected examples are given in Figure 1, including SDZ-216525 (a 5-HT_7 selective agonist),[2] Delavirdine (a non-nucleoside reverse

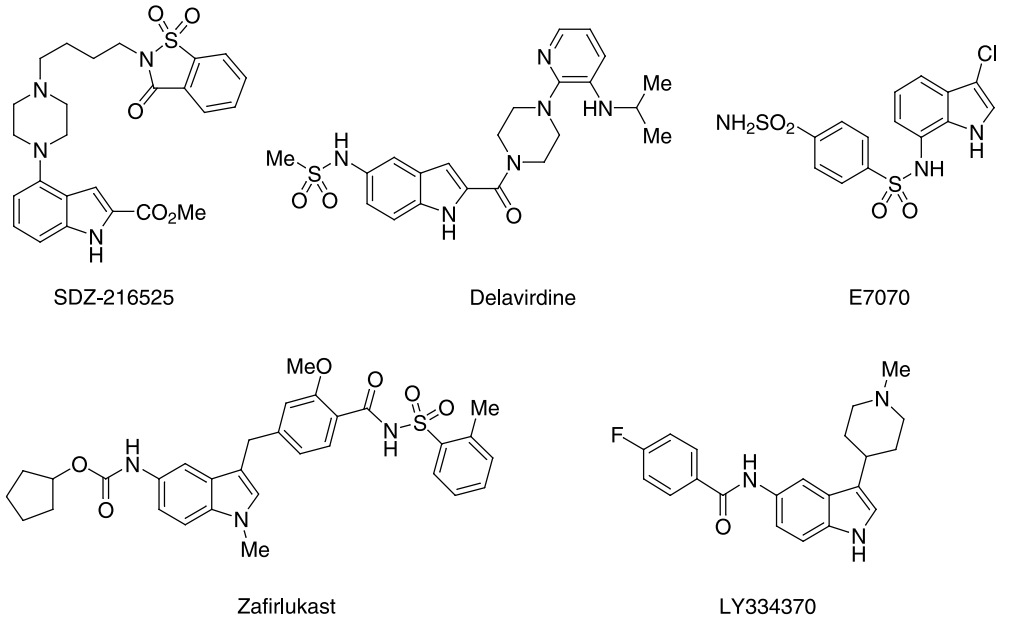

Figure 1. Selected bioactive indoles possessing a nitrogen-based substituent.

☆ Part 4 of Chemistry of Aminophenols. Some of the results were communicated in a preliminary report, see Ref. 20j.

Keywords: Cross-coupling; Heteroannulation; Nitroindoles; Aryl triflates; 2-Aminophenols.
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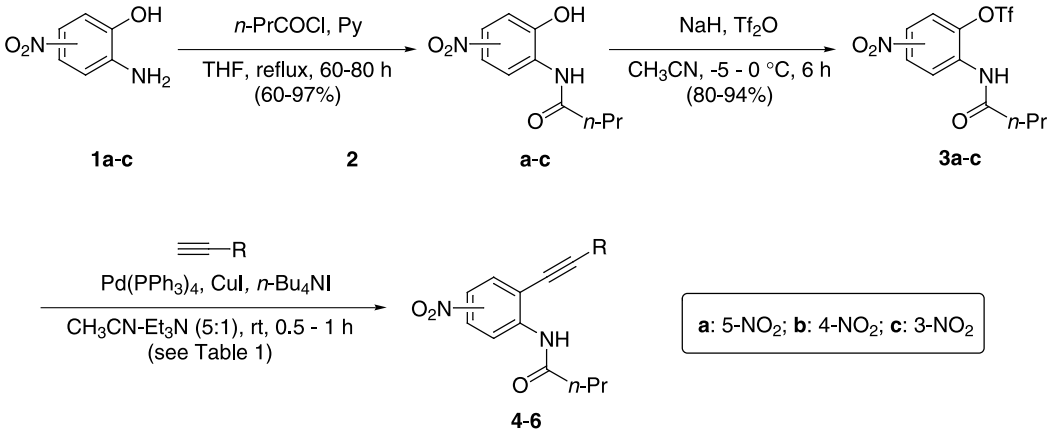
doi:10.1016/j.tet.2004.09.034



Scheme 1. Synthesis of 2-alkynylanilines **4**–**6**.

transcriptase inhibitor approved for HIV therapy),[3] Zafirlukast (an LTD_4 antagonist),[4] LY334370 (a selective 5-HT_{1F} receptor agonist),[5] and E7070 (an anticancer agent thought to affect the progression of the cell cycle in the G1 phase with inhibition of expression of cyclin E and phosphorylation of cdk2).[6] Direct nitration of indoles is a straightforward method for synthesis of nitroindoles,[1,7] but it suffers from non-selectivity in some cases.[1] A number of methodologies[8] have been used to form nitroindoles. These cover the Fischer indole synthesis,[9] the Bergman indole synthesis,[10] and various nucleophilic/electrophilic cyclization approaches by using the nitro-containing substrates.[11] However, low yields and/or formation of mixtures of nitroindoles were reported.[9e,f,11c–e]

The metal-catalyzed cross-coupling reactions have emerged as the most powerful methods for carbon–carbon bond formation in recent years and they have been used for heterocycle synthesis.[12] Among the metal-catalyzed indole syntheses,[8] the cross-coupling and heteroannulation procedures enjoy wide applications. 2-Haloanilines and derivatives are the common substrates, which are transformed into 2-alkynylanilines via Pd(0)–Cu(I)-catalyzed Sonogashira cross-coupling with 1-alkynes[13] followed by metal-catalyzed,[13–19] or base-[20–22] and iodonium(I)-mediated[23] heteroannulation. Alternatively, 2-alkynylanilines undergo aminopalladation–reductive elimination with aryl/vinyl iodides and triflates to form highly functionalized indoles.[24,25] Moreover, 2-iodoanilines react with internal alkynes via Pd-catalyzed annulation to afford 2,3-disubstituted indoles (Larock indole synthesis).[14,26] There are two reports on synthesis of C5- and C7-nitroindoles through the cross-coupling and heteroannulation procedures.[17f,20h,k] In both cases, 2-iodo nitroanilines were used as the starting materials, which were synthesized from nitroanilines by using bis(pyridine)iodonium(I) tetrafluoroborate (IPy_2BF_4) as the iodinating agent.[17f] The nitro-containing 2-alkynylanilines cyclized to nitroindoles via CuI- and *t*-BuOK-mediated heteroannulation, respectively.[17f,20h,k] We report here on a general and efficient synthesis of 2-substituted C5-, C6-, and C7-nitroindoles starting from commercially available 2-amino nitrophenols.[20j]

2. Results and discussion

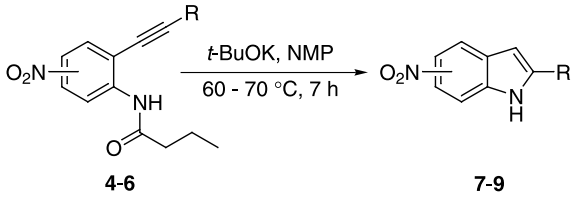
2-Iodoanilines could be prepared from 4-substituted anilines by using IPy_2BF_4 as the iodinating agent.[17f] However, the C4 substituent is necessary for directing the iodination at C2.[27] Alternatively, the oxygen-substituted 2-iodoanilines could be prepared from protected aminophenols by directed *ortho*-lithiation followed by trapping with I_2.[20g] We used the nitro 2-trifloxyanilides **3** to substitute 2-iodoanilines in the metal-catalyzed indole synthesis. Before our work,[20i,j] a 2-trifloxyanilide was used for the Pd-catalyzed cross-coupling with alkynylstannanes to provide 2-alkynylanilides.[15g] The Pd(0)–Cu(I)-catalyzed Sonogashira cross-coupling of 2-trifloxyanilides with 1-alkynes was virtually unknown. We found a remarkable additive effect on the cross-coupling of 2-trifloxyanilides with 1-alkynes and high yields of 2-alkynylanilides were obtained in the presence of 1.5 equiv of *n*-Bu_4NI.[20i] As shown in Scheme 1, three nitro 2-trifloxyanilides **3a**–**c** were readily prepared from 2-amino-5-nitrophenol (**1a**), 2-amino-4-nitrophenol (**1b**), and 2-amino-3-nitrophenol (**1c**) via selective N-acylation[28] followed by formation of triflates from **2a**–**c**. The butyryl anilides were selected for their relatively good solubility in common organic solvents compared with the acetamides. Cross-coupling of **3a**–**c** with 1-alkynes took place at room temperature in CH_3CN–Et_3N (5:1) with 1.5 equiv of *n*-Bu_4NI as the additive to give the 2-alkynyl nitroanilides **4**–**6** in excellent yields. The results are summarized in Table 1.

Table 1. Cross-coupling of aryl triflates **3** with 1-alkynes[a]

Entry	Aryl triflate	R	Yield (%)
1	**3a**: 5-NO_2	Ph	**4a**: 95
2	**3a**: 5-NO_2	*n*-Pr	**4b**: 95
3	**3b**: 4-NO_2	Ph	**5a**: 96
4	**3b**: 4-NO_2	*n*-Pr	**5b**: 90
5	**3c**: 3-NO_2	Ph	**6a**: 90
6	**3c**: 3-NO_2	*n*-Pr	**6b**: 91

[a] Carried out with 10 mol% $Pd(PPh_3)_4$, 30 mol% CuI, and 150 mol% *n*-Bu_4NI.

Table 2. Synthesis of nitroindoles **7–9** via *t*-BuOK-mediated heteroannulation[a]



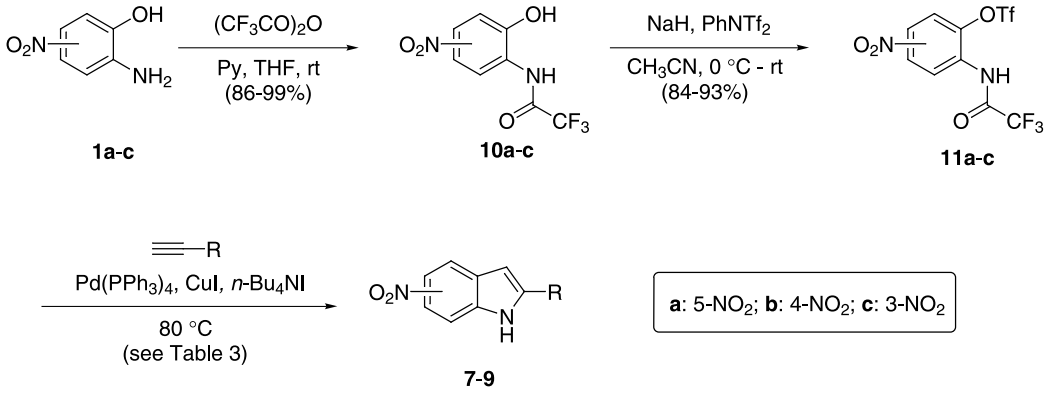
4-6 **7-9**

Entry	Nitroindoles	R	Yield (%)
1	5-NO_2	Ph	**7a**: 85
2	5-NO_2	*n*-Pr	**7b**: 84
3	6-NO_2	Ph	**8a**: 84
4	6-NO_2	*n*-Pr	**8b**: 86
5	7-NO_2	Ph	**9a**: 76
6	7-NO_2	*n*-Pr	**9b**: 72

[a] 1.2 equiv of *t*-BuOK were used.

Heteroannulation of 2-alkynyl nitroanilides **4–6** was carried out in NMP with 1.2 equiv of *t*-BuOK at 60–70 °C for 7 h to furnish 2-substituted C5-, C6-, and C7-nitroindoles **7–9** in 72–86% yields (Table 2). In Knochel's nitroindole synthesis, a unprotected 2-alkynylaniline was used.[20h] We found that the *N*-acyl group, the position of nitro group, and the nature of R in **4–6** did not affect the efficiency of the base-mediated heteroannulation.[29] Nitroindoles **7–9** are all crystalline compounds; the C6-nitroindole **8b** was analyzed by X-ray crystallography, showing a flat nitroindole skeleton.[30]

Next, we examined a one-pot cross-coupling and heteroannulation procedure toward nitroindoles **7–9** as shown in Scheme 2. A Cu(I)-catalyzed one-pot synthesis of indoles from 2-iodotrifluoroacetanilide and 1-alkynes was recently reported.[17h] In our nitroindole synthesis, the trifluoroacetamidoaryl triflates **11a–c** were prepared in good yields by selective N-acylation of **1a–c** followed by triflate formation from **10a–c** and $PhNTf_2$. The one-pot cross-coupling and heteroannulation of **10a–c** with various 1-alkynes was investigated and the results are given in Table 3. We observed solvent effect on the one-pot reactions and used three solvent combinations, A (DMF–Et_3N=5:1), B (CH_3CN–Et_3N=5:1), and C (DMF–TMG=5:1). For formation of C5- and C6-nitroindoles **7** and **8** (entries 1–10, Table 3), solvents A and B could be used and the product yields are comparable to those given in Table 2. However, the one-pot reaction times were significantly prolonged than the stepwise protocol. Under the one-pot reaction conditions, some functional groups such as OH, CN, and Cl remained intact and protection of OH was not required. Formation of C7-nitroindoles **9** by the one-pot procedure was somewhat problematic. After screening on catalyst precursor, solvent, and base, three C7-nitroindoles **9a–c** could be obtained albeit in lower yields (entries 11–13,



Scheme 2. One-pot synthesis of nitroindoles **7–9**.

Table 3. One-pot synthesis of nitroindoles via Pd-catalyzed coupling and heteroannulation[a]

Entry	Nitroindoles	R	*t* (h)	Yield (%)
1	5-NO_2	Ph	41	**7a**: 85
2	5-NO_2	*n*-Pr	24	**7b**: 90
3[b]	5-NO_2	$(CH_2)_2OH$	42	**7c**: 68
4	5-NO_2	$(CH_2)_3CN$	25	**7d**: 75
5[b]	5-NO_2	$(CH_2)_3Cl$	24	**7e**: 45
6[b]	6-NO_2	Ph	17	**8a**: 88
7	6-NO_2	*n*-Pr	21	**8b**: 84
8	6-NO_2	$(CH_2)_2OH$	19	**8c**: 69
9	6-NO_2	$(CH_2)_3CN$	8	**8d**: 73
10[b]	6-NO_2	$(CH_2)_3Cl$	20	**8e**: 66
11[c–e]	7-NO_2	Ph	3.5	**9a**: 52
12[c,d]	7-NO_2	*n*-Pr	7.5	**9b**: 39
13[d]	7-NO_2	$(CH_2)_2OH$	12	**9c**: 48

[a] Carried out in solvent A (DMF–Et_3N=5:1) with 10 mol% $Pd(PPh_3)_4$, 30 mol% CuI, and 150 mol% *n*-Bu_4NI.
[b] Carried out in solvent B (CH_3CN–Et_3N=5:1).
[c] Carried out in solvent C (DMF–TMG=5:1).
[d] $Pd(PPh_3)_2Cl_2$ was used to replace $Pd(PPh_3)_4$.
[e] Carried out at 100 °C. TMG=1,1,3,3-tetramethylguanidine.

Table 3). Use of $Pd(PPh_3)_2Cl_2$ as the catalyst precursor seems essential along with a stronger base, TMG. Higher reaction temperature (100 °C) was also applied for the formation of **9a**. These results suggest that the *ortho* nitro group in **11c** may form hydrogen bond with the amido moiety, thus interfering the indole ring closure reaction. This type of intramolecular hydrogen bond would be destroyed when a strong base such as *t*-BuOK was used for the heteroannulation. Therefore, no difference was recognized among the stepwise synthesis of C5-, C6-, and C7-nitroindoles.

3. Conclusion

In summary, we have established general and efficient cross-coupling–heteroannulation procedures toward 2-substituted C5-, C6-, and C7-nitroindoles starting from the commercially available 2-amino nitrophenols. Both stepwise and one-pot protocols were examined and the former approach seems much more reliable and tolerant to the position of nitro group on the benzene ring. Nitroindoles can be converted, by hydrogenation over Pd/C, into aminoindoles,[20j] which are useful precursors to a variety of indole derivatives possessing nitrogen-based ring substituents.

4. Experimental

^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ or acetone-d_6 (300 MHz for ^1H and 75 MHz for ^{13}C, respectively) with $CHCl_3$ or acetone as the internal reference. IR spectra were taken on a FT-IR spectrophotometer. Mass spectra (MS) were measured by the +CI method. Elemental analyses were performed by Zhejiang University and Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences. All reactions were carried out under a nitrogen atmosphere and monitored by thin-layer chromatography on 0.25-mm E. Merck silica gel plates (60 F-254) using UV light, or 7% ethanolic phosphomolybdic acid and heating as the visualizing methods. E. Merck silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography. Yields refer to chromatographically and spectroscopically (^1H NMR) homogeneous materials. Reagents were obtained commercially and used as received. Room temperature is around 20 °C.

4.1. Representative procedure for the acylation of 2-amino nitrophenols 1a–c

4.1.1. *N*-(2′-Hydroxy-5′-nitrophenyl)butyramide (2b). To a solution of 2-amino-4-nitrophenol **1b** (462.0 mg, 3.00 mmol) in dry THF (25 mL) cooled in an ice-water bath was added pyridine (0.30 mL, 3.80 mmol) and butyryl chloride (0.34 mL, 3.30 mmol) through a syringe, respectively. The resultant mixture was stirred for 60 h at refluxing temperature under a nitrogen atmosphere. The reaction was quenched by water and the resultant mixture was extracted with EtOAc (30×3 mL). The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, and evaporated under reduced pressure. The residue was purified by flash column chromatography (silica gel, 25% EtOAc in hexane) to give **2b** (650.0 mg, 97%) as a pale yellow crystalline solid; mp 191–192 °C (CH_2Cl_2–hexane); R_f=0.53 (33% EtOAc in hexane); IR (film) 3406, 1646, 1529, 1498, 1343, 1289 cm^{-1}; ^1H NMR (300 MHz, acetone-d_6) δ 10.85 (br s, 1H), 9.24 (br s, 1H), 8.99 (d, J=2.8 Hz, 1H), 8.06 (dd, J=8.9, 2.8 Hz, 1H), 7.20 (d, J=9.0 Hz, 1H), 2.68 (t, J=7.4 Hz, 2H), 1.88 (sextet, J=7.4 Hz, 2H), 1.13 (t, J=7.4 Hz, 3H); ^{13}C NMR (75 MHz, acetone-d_6) δ 172.8, 152.8, 140.2, 126.9, 120.2, 116.3, 115.8, 37.9, 18.4, 12.7; MS (+CI) m/z 225 ($M+H^+$, 100). Anal. Calcd for $C_{10}H_{12}N_2O_4$: C, 53.57; H, 5.39; N, 12.49. Found: C, 53.81; H, 5.40; N, 12.31%.

4.1.2. *N*-(2′-Hydroxy-4′-nitrophenyl)butyramide (2a). Prepared in 86% yield from 2-amino-5-nitrophenol **1a**. *Compound* **2a**. A colorless crystalline solid; mp 175–176 °C (CH_2Cl_2–hexane); R_f=0.51 (50% EtOAc in hexane); IR (film) 3409, 1664, 1504, 1421, 1341 cm^{-1}; ^1H NMR (300 MHz, acetone-d_6) δ 9.22 (br s, 1H), 8.36 (d, J=8.8 Hz, 1H), 7.94–7.87 (m, 2H), 2.69 (t, J=7.4 Hz, 2H), 1.87 (sextet, J=7.4 Hz, 2H), 1.12 (t, J=7.4 Hz, 3H); ^{13}C NMR (75 MHz, acetone-d_6) δ 172.5, 146.3, 143.2, 133.2, 119.6, 115.4, 110.1, 38.1, 18.3, 12.7; MS (+CI) m/z 225 ($M+H^+$, 100). Anal. Calcd for $C_{10}H_{12}N_2O_4$: C, 53.57; H, 5.39; N, 12.49. Found: C, 53.62; H, 5.48; N, 12.38%.

4.1.3. *N*-(2′-Hydroxy-6′-nitrophenyl)butyramide (2c). Prepared in 60% yield from 2-amino-3-nitrophenol **1c** using NaH to replace pyridine as the base (room temperature, 24 h). *Compound* **2c**. A yellow crystalline solid; mp 119–120 °C (CH_2Cl_2–hexane); R_f=0.34 (25% EtOAc in hexane); IR (film) 3395, 3141 (br), 1663, 1540, 1511, 1367 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.09 (br s, 1H), 9.32 (s, 1H), 7.71 (dd, J=8.4, 1.5 Hz, 1H), 7.36 (dd, J=8.2, 1.5 Hz, 1H), 7.24 (t, J=8.3 Hz, 1H), 2.56 (t, J=7.4 Hz, 2H), 1.82 (sextet, J=7.4 Hz, 2H), 1.04 (t, J=7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.0, 151.2, 141.2, 127.1, 126.1, 122.2, 117.9, 39.4, 19.0, 13.5; MS (+CI) m/z 225 ($M+H^+$, 100). Anal. Calcd for $C_{10}H_{12}N_2O_4$: C, 53.57; H, 5.39; N, 12.49. Found: C, 53.72; H, 5.45; N, 12.42%.

4.2. Representative procedure for the synthesis of nitroaryl triflates using NaH as the base

4.2.1. *N*-[5′-Nitro-2′-(((trifluoromethane)sulfonyl)oxy)-phenyl]butyramide (3b). To a suspension of NaH (60%, 8.0 mg, 2.03 mmol) in dry MeCN (15 mL) cooled in an ice-water bath under a nitrogen atmosphere was added a solution of **2b** (363.0 mg, 1.62 mmol) in dry MeCN (30 mL) followed by stirring at the same temperature for 20 min. Tf_2O (0.30 mL, 1.78 mmol) was then added dropwise, and the resultant mixture was stirred for 6 h at −5–0 °C. The reaction was quenched by water and the resultant mixture was extracted with EtOAc (30×2 mL). The combined organic layer was washed with 5% aqueous HCl, saturated aqueous $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$, and evaporated under reduced pressure. The residue was purified by flash column chromatography (silica gel, 25% EtOAc in hexane) to give **3b** (461.0 mg, 80%) as a white crystalline solid; mp 73–74 °C (CH_2Cl_2–hexane); R_f=0.51 (25% EtOAc in hexane); IR (film) 3271 (br), 2969, 1681, 1542, 1430, 1217 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ

9.30 (d, J=2.7 Hz, 1H), 8.04 (dd, J=9.0, 2.7 Hz, 1H), 7.55–7.47 (br s, 1H), 7.48 (d, J=9.0 Hz, 1H), 2.45 (t, J=7.4 Hz, 2H), 1.79 (sextet, J=7.4 Hz, 2H), 1.03 (t, J=7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3, 148.6, 141.9, 131.6, 122.1, 119.6, 118.5, 118.3 (q, J_{C-F}=318.4 Hz), 39.4, 18.5, 13.6; MS (+CI) m/z 357 ($M+H^+$, 100). Anal. Calcd for $C_{11}H_{11}F_3N_2O_6S$: C, 37.08; H, 3.11; N, 7.86. Found: C, 37.45; H, 3.13; N, 7.77%.

4.2.2. *N*-[4′-Nitro-2′-(((trifluoromethane)sulfonyl)oxy)-phenyl]butyramide (3a). Prepared from **2a** in 87% yield. *Compound* **3a**. A colorless crystalline solid; mp 88–89 °C (EtOAc); R_f=0.45 (25% EtOAc in hexane); IR (film) 3274 (br), 2972, 1690, 1516, 1435, 1350, 1217 cm^{-1}; ^{1}H NMR (300 MHz, acetone-d_6) δ 9.68 (br s, 1H), 8.68–8.48 (m, 3H), 2.70 (t, J=7.4 Hz, 2H), 1.88 (sextet, J=7.4 Hz, 2H), 1.12 (t, J=7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.5, 142.7, 138.8, 136.8, 123.9, 123.6, 118.3 (q, J_{C-F}=318.4 Hz), 117.4, 38.0, 17.9, 12.7; MS (+CI) m/z 357 ($M+H^+$, 100). Anal. Calcd for $C_{11}H_{11}F_3N_2O_6S$: C, 37.08; H, 3.11; N, 7.86. Found: C, 37.40; H, 3.21; N, 7.66%.

4.3. Procedure for the synthesis of nitroaryl triflate using Et_3N as the base

4.3.1. *N*-[6′-Nitro-2′-(((trifluoromethane)sulfonyl)oxy)-phenyl]butyramide (3c). To a solution of **2c** (395.0 mg, 1.76 mmol) and Et_3N (0.30 mL, 2.20 mmol) in dry CH_2Cl_2 (20 mL) cooled in an ice-water bath under a nitrogen atmosphere was added Tf_2O (0.33 mL, 1.93 mmol) dropwise. The resultant mixture was stirred at the same temperature for 7 h. After removal of CH_2Cl_2 under reduced pressure, the residue was dissolved in 25 mL EtOAc and then washed with 5% aqueous HCl, saturated aqueous $NaHCO_3$, and brine. The organic layer was dried over anhydrous $MgSO_4$ and evaporated under reduced pressure. The residue was purified by flash column chromatography (silica gel, 25% EtOAc in hexane) to give **3c** (590.0 mg, 94%) as a white crystalline sold; mp 119–119.5 °C (CH_2Cl_2–hexane); R_f=0.40 (25% EtOAc in hexane); IR (film) 3248 (br), 2973, 1676, 1541, 1518, 1425, 1209 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18 (br s, 1H), 8.10 (dd, J=8.4, 1.4 Hz, 1H), 7.62 (dd, J=8.4, 1.4 Hz, 1H), 7.48 (t, J=8.4 Hz, 1H), 2.46 (t, J=7.4 Hz, 2H), 1.77 (sextet, J=7.4 Hz, 2H), 1.02 (t, J=7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2, 145.1, 145.0, 127.5, 126.9, 126.1, 124.9, 118.4 (q, J_{C-F}=318.5 Hz), 38.5, 18.4, 13.6; MS (+CI) m/z 357 ($M+H^+$, 100). Anal. Calcd for $C_{11}H_{11}F_3N_2O_6S$: C, 37.08; H, 3.11; N, 7.86. Found: C, 37.16; H, 3.15; N, 8.06%.

4.4. Representative procedure for the cross-coupling of triflates with 1-alkynes

4.4.1. *N*-[(5′-Nitro-2′-phenylethynyl)phenyl]butyramide (5a). To a suspension of triflate **3b** (142.0 mg, 0.40 mmol), $Pd(PPh_3)_4$ (46.0 mg, 4.0×10^{-2} mmol), CuI (23.0 mg, 0.12 mmol), and n-Bu_4NI (222.0 mg, 0.60 mmol) in degassed dry MeCN (5 mL) was added Et_3N (1.0 mL) and phenylacetylene (90 μL, 0.80 mmol), respectively, through a syringe under a nitrogen atmosphere. The resultant mixture was stirred at room temperature for 1 h. The reaction was quenched by saturated aqueous NH_4Cl and the resultant mixture was extracted with EtOAc (20×2 mL). The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, 30% EtOAc in hexane) to give **5a** (126.0 mg, 96%) as a yellow crystalline solid; mp 168–169 °C (CH_2Cl_2–hexane); R_f=0.44 (25% EtOAc in hexane); IR (film) 3290, 2960, 2214, 1665, 1534, 1341 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.36 (d, J=2.2 Hz, 1H), 8.09 (br s, 1H), 7.92 (dd, J=8.5, 2.2 Hz, 1H), 7.62 (d, J=8.5 Hz, 1H), 7.58–7.55 (m, 2H), 7.47–7.40 (m, 3H), 2.47 (t, J=7.4 Hz, 2H), 1.82 (sextet, J=7.4 Hz, 2H), 1.05 (t, J=7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3, 147.9, 139.5, 132.0, 131.7 (×2), 129.9, 128.8 (×2), 121.2, 118.0, 117.8, 114.3, 100.8, 82.8, 39.8, 18.8, 13.7; MS (+CI) m/z 309 ($M+H^+$, 100). Anal. Calcd for $C_{18}H_{16}N_2O_3$: C, 70.12; H, 5.23; N, 9.09. Found: C, 69.75; H, 6.00; N, 9.20%.

4.4.2. *N*-[(4′-Nitro-2′-phenylethynyl)phenyl]butyramide (4a). Prepared from the triflate **3a** and 1-phenylacetylene in 95% yield. *Compound* **4a**. A colorless crystalline solid; mp 149–150 °C (CH_2Cl_2–hexane); R_f=0.54 (25% EtOAc in hexane); IR (film) 3306, 2959, 2212, 1677, 1574, 1506 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.68 (d, J=9.2 Hz, 1H), 8.38 (d, J=2.6 Hz, 1H), 8.25 (br s, 1H), 8.20 (dd, J=8.6, 2.6 Hz, 1H), 7.58–7.55 (m, 2H), 7.47–7.40 (m, 3H), 2.49 (t, J=7.4 Hz, 2H), 1.82 (sextet, J=7.4 Hz, 2H), 1.05 (t, J=7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.4, 143.9, 142.6, 131.6 (×2), 129.7, 128.8 (×2), 127.1, 125.2, 121.2, 118.7, 112.3, 98.5, 82.02, 40.0, 18.8, 13.7; MS (+CI) m/z 309 ($M+H^+$, 100). Anal. Calcd for $C_{18}H_{16}N_2O_3$: C, 70.12; H, 5.23; N, 9.09. Found: C, 70.34; H, 5.63; N, 8.87%.

4.4.3. *N*-[(4′-Nitro-2′-(pentyn-1″-yl))phenyl]butyramide (4b). Prepared from the triflate **3a** and 1-pentyne in 95% yield. *Compound* **4b**. A white crystalline solid; mp 87–88 °C (CH_2Cl_2–hexane); R_f=0.59 (25% EtOAc in hexane); IR (film) 3335, 2965, 2228, 1678, 1503, 1345 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.59 (d, J=9.2 Hz, 1H), 8.23–8.15 (br s, 1H), 8.19 (d, J=2.6 Hz, 1H), 8.09 (dd, J=9.2, 2.6 Hz, 1H), 2.51 (t, J=7.0 Hz, 2H), 2.42 (t, J=7.4 Hz, 2H), 1.81–1.65 (m, 4H), 1.08 (t, J=7.4 Hz, 3H), 1.02 (t, J=7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.4, 144.0, 142.3, 126.9, 124.4, 118.2, 112.9, 100.3, 74.2, 39.9, 21.9, 21.4, 18.7, 13.6, 13.5; MS (+CI) m/z 275 ($M+H^+$, 100). Anal. Calcd for $C_{15}H_{18}N_2O_3$: C, 65.68; H, 6.61; N, 10.21. Found: C, 66.03; H, 6.73; N, 10.05%.

4.4.4. *N*-[(5′-Nitro-2′-(pentyn-1″-yl))phenyl]butyramide (5b). Prepared from the triflate **3b** and 1-pentyne in 90% yield. *Compound* **5b**. A white crystalline solid; mp 91–92 °C (CH_2Cl_2–hexane); R_f=0.38 (25% EtOAc in hexane); IR (film) 3290, 2962, 2223, 1668, 1529, 1344 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.31 (d, J=2.2 Hz, 1H), 8.04 (br s, 1H), 7.85 (dd, J=8.5, 2.2 Hz, 1H), 7.47 (d, J=8.5 Hz, 1H), 2.55 (t, J=7.0 Hz, 2H), 2.42 (t, J=7.4 Hz, 2H), 1.82–1.67 (m, 4H), 1.11 (t, J=7.4 Hz, 3H), 1.04 (t, J=7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2, 147.4, 139.5, 131.9, 118.5, 117.8, 113.9, 102.9, 75.0, 39.8, 21.9, 21.6, 18.8, 13.7, 13.6; MS (+CI) m/z 275 ($M+H^+$, 100). Anal. Calcd for $C_{15}H_{18}N_2O_3$: C, 65.68; H, 6.61; N, 10.21. Found: C, 65.48; H, 6.79; N, 9.86%.

4.4.5. *N*-[(6′-Nitro-2′-phenylethynyl)phenyl]butyramide (6a). Prepared from the triflate **3c** and 1-phenylacetylene in 90% yield. *Compound* **6a**. A white crystalline solid; mp 167–168 °C (CH_2Cl_2–hexane); R_f=0.31 (25% EtOAc in hexane); IR (film) 3275, 2923, 2215, 1668, 1509 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.13 (br s, 1H), 7.89 (dd, J=8.3, 1.4 Hz, 1H), 7.76 (dd, J=8.3, 1.4 Hz, 1H), 7.53–7.48 (m, 2H), 7.42–7.35 (m, 3H), 7.29 (t, J=8.1 Hz, 1H), 2.44 (t, J=7.4 Hz, 2H), 1.78 (sextet, J=7.4 Hz, 2H), 1.01 (t, J=7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 144.3, 136.7, 131.6 (×2), 131.4, 129.3, 128.6 (×2), 125.3, 124.9, 121.8, 120.9, 97.2, 83.7, 38.9, 18.8, 13.7; MS (+CI) *m/z* 309 ($M+H^+$, 100). Anal. Calcd for $C_{18}H_{16}N_2O_3$: C, 70.12; H, 5.23; N, 9.09. Found: C, 70.31; H, 5.91; N, 8.82%.

4.4.6. *N*-[(6′-Nitro-2′-(pentyn-1″-yl))phenyl]butyramide (6b). Prepared from the triflate **3c** and 1-pentyne in 91% yield. *Compound* **6b**. A white crystalline solid; mp 144–145 °C (CH_2Cl_2–hexane); R_f=0.36 (25% EtOAc in hexane); IR (film) 3272, 2961, 2225, 1670, 1511, 1536 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.95 (br s, 1H), 7.79 (dd, J=8.0, 1.4 Hz, 1H), 7.60 (dd, J=8.0, 1.4 Hz, 1H), 7.20 (t, J=8.0 Hz, 1H), 2.44 (t, J=7.0 Hz, 2H), 2.39 (t, J=7.4 Hz, 2H), 1.83–1.56 (m, 4H), 1.05 (t, J=7.3 Hz, 3H), 1.01 (t, J=7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 144.3, 136.4, 131.0, 124.9, 124.2, 121.0, 99.2, 75.3, 38.7, 21.9, 21.4, 18.7, 13.6, 13.5; MS (+CI) *m/z* 275 ($M+H^+$, 100). Anal. Calcd for $C_{15}H_{18}N_2O_3$: C, 65.68; H, 6.61; N, 10.21. Found: C, 64.19; H, 6.05; N, 10.50%.

4.5. Representative procedure for the synthesis of trifluoroacetanilides 10a–c

4.5.1. *N*-(2′-Hydroxy-5′-nitrophenyl)trifluoroacetamide (10b). To a solution of 2-amino-4-nitrophenol **1b** (3.124 g, 20 mmol) in dry THF (83 mL) and pyridine (2.4 mL, 29.95 mmol) cooled in an ice-water bath was added dropwise a solution of trifluoroacetic anhydride (3.1 mL, 22 mmol) in dry THF (7 mL). The resultant mixture was stirred for 16 h at room temperature under a nitrogen atmosphere. The reaction was quenched by adding water (10 mL) and brine (10 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (20×2 mL). The combined organic layer was washed with 5% HCl (15 mL), saturated aqueous $NaHCO_3$ (20 mL), and brine (20 mL), dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, 50% EtOAc in hexane) to give **10b** (5.000 g, 99%) as a yellow crystalline solid; mp 188–189 °C (EtOAc–hexane); R_f=0.30 (50% EtOAc in hexane); IR (KBr): 3386, 3188 (br), 1696 cm^{-1}; ^1H NMR (300 MHz, acetone-d_6) δ 11.20–10.30 (br s, 1H), 9.90–9.55 (br s, 1H), 9.02 (d, J=2.7 Hz, 1H), 8.22 (dd, J=9.1, 2.8 Hz, 1H), 7.34 (d, J=9.0 Hz, 1H); ^{13}C NMR (75 MHz, acetone-d_6) δ 153.7, 146.6, 140.0, 123.4, 122.4, 118.0, 115.4 (q, J_{C-F}=287.1 Hz), 114.9; MS (+CI) *m/z* 251 ($M+H^+$,100). Anal. Calcd for $C_8H_5F_3N_2O_4$: C, 38.41; H, 2.01; N, 11.20. Found: C, 38.32; H, 1.88; N, 11.00%.

4.5.2. *N*-(2′-Hydroxy-4′-nitrophenyl)trifluoroacetamide (10a). Prepared in 99% yield from 2-amino-5-nitrophenol **1a** after reaction at room temperature for 4 h. *Compound* **10a**. As a yellow crystalline solid; mp 164–165 °C (EtOAc–hexane); R_f=0.32 (25% EtOAc in hexane); IR (KBr) 3374, 3222 (br), 1697 cm^{-1}; ^1H NMR (300 MHz, acetone-d_6) δ 10.60–9.35 (br s, 2H), 8.40 (d, J=8.7 Hz, 1H), 8.02–7.90 (m, 2H); ^{13}C NMR (75 MHz, acetone-d_6) δ 154.7 (q, J_{C-F}=45.3 Hz), 147.7, 145.1, 129.7, 121.5, 115.6 (q, J_{C-F}=271.7 Hz), 115.2, 109.7; MS (+CI) *m/z* 251 ($M+H^+$, 100). Anal. Calcd for $C_8H_5F_3N_2O_4$: C, 38.41; H, 2.01; N, 11.20. Found: C, 38.15; H, 1.94; N, 11.39%.

4.5.3. *N*-(2′-Hydroxy-6′-nitrophenyl)trifluoroacetamide (10c). Prepared in 86% yield from 2-amino-3-nitrophenol **1c** after reaction at room temperature for 9 h. *Compound* **10c**. As a yellow crystalline solid; mp 136–137 °C (EtOAc–hexane); R_f=0.41 (50% EtOAc in hexane); IR (KBr) 3310 (br), 1729 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 11.04 (br s, 1H), 8.05–7.75 (br s, 1H), 7.85 (dd, J=7.8, 2.1 Hz, 1H), 7.47–7.38 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 153.4 (q, J_{C-F}=43.5 Hz), 146.4, 146.0, 128.5, 120.7, 115.3, 115.5 (q, J_{C-F}=286.8 Hz), 115.0; MS (+CI) *m/z* 251 ($M+H^+$, 100). Anal. Calcd for $C_8H_5F_3N_2O_4$: C, 38.41; H, 2.01; N, 11.20. Found: C, 38.41; H, 1.85; N, 10.80%.

4.6. Representative procedure for the synthesis of nitroaryl triflates 11a–c

4.6.1. *N*-[5′-Nitro-2′-(((trifluoromethane)sulfonyl)oxy)-phenyl]trifluoroacetamide (11b). To a suspension of NaH (0.54 g, 13.5 mmol) in dry THF (80 mL) cooled in an ice-water bath was added dropwise a solution of **10b** (2.25 g, 9.0 mmol) and $PhNTf_2$ (4.82 g, 13.5 mmol) in dry THF (20 mL). The resultant mixture was stirred for 19 h at room temperature under a nitrogen atmosphere. The reaction was quenched by water (25 mL) and brine (25 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ (45 mL×5) and brine (35 mL), dried over anhydrous Na_2SO_4, evaporated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, 25% EtOAc in hexane) to give **11b** (3.20 g, 93%) as a yellow crystalline solid; mp 88–89 °C (EtOAc–hexane); R_f=0.54 (25% EtOAc in hexane); IR (KBr) 3292 (br), 1717 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.17 (d, J=2.7 Hz, 1H), 8.28 (br s, 1H), 8.24 (dd, J=9.3, 3.0 Hz, 1H), 7.62 (d, J=9.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.9 (q, J_{C-F}=39.4 Hz), 148.0, 143.8, 129.4, 123.7, 123.2, 120.1, 119.2 (q, J_{C-F}=320.9 Hz), 115.8 (q, J_{C-F}=288.4 Hz); MS (+CI) *m/z* 383 ($M+H^+$, 100). Anal. Calcd for $C_9H_4F_6N_2O_6S$: C, 28.28; H, 1.05; N, 7.33. Found: C, 28.39; H, 0.89; N, 6.65%.

4.6.2. *N*-[4′-Nitro-2′-(((trifluoromethane)sulfonyl)oxy)-phenyl]trifluoroacetamide (11a). Prepared from **10a** in 84% yield after reaction at room temperature for 4 h. *Compound* **11a**. As a yellow crystalline solid; mp 66–67 °C (EtOAc–hexane); R_f=0.38 (25% EtOAc in hexane); IR (KBr) 3284, 1725 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.62 (d, J=9.3 Hz, 1H), 8.46–8.32 (br s, 1H), 8.38 (dd, J=9.0, 2.7 Hz, 1H), 8.31 (d, J=2.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.8 (q, J_{C-F}=45.1 Hz), 145.4, 138.3, 134.1, 125.4, 123.5, 119.1 (q, J=320.2 Hz), 118.8, 117.2 (q, J=288.1 Hz); MS (+CI) *m/z* 383 ($M+H^+$, 100). Anal. Calcd for $C_9H_4F_6N_2O_6S$: C, 28.28; H, 1.05; N, 7.33. Found: C, 28.53; H, 0.98; N, 6.86%.

4.6.3. *N*-[6′-Nitro-2′-(((trifluoromethane)sulfonyl)oxy)-phenyl]trifluoroacetamide (11c). Prepared from **10c** in 88% yield after reaction at room temperature for 24 h. *Compound* **11c**. As a yellow crystalline solid; mp 108.5–109.5 °C; R_f=0.37 (25% EtOAc in hexane); IR (KBr) 3255, 1732 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.10 (br s, 1H), 8.22 (dd, J=8.2, 1.3 Hz, 1H), 7.75 (dd, J=8.4, 1.5 Hz, 1H), 7.66 (t, J=8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.1 (q, J_{C-F}=43.2 Hz), 145.6, 145.3, 129.8, 129.1, 126.1, 123.6, 119.1 (q, J_{C-F}=320.6 Hz), 115.9 (q, J_{C-F}=288.2 Hz); MS (+CI) m/z 383 ($M+H^+$, 100). Anal. Calcd for $C_9H_4F_6N_2O_6S$: C, 28.28; H, 1.05; N, 7.33. Found: C, 28.34; H, 0.96; N, 7.25%.

4.7. Representative procedure for the *t*-BuOK-promoted heteroannualtion toward nitroindoles

4.7.1. 6-Nitro-2-phenylindole (8a). A mixture of **5a** (60.0 mg, 0.19 mmol), *t*-BuOK (25.0 mg, 0.22 mmol) in dry NMP (2.0 mL) was heated at 60–70 °C for 7 h under a nitrogen atmosphere. After cooling to room temperature, water (2 mL) and EtOAc (50 mL) were added to the reaction mixture, respectively. The separated aqueous layer was extracted with EtOAc (20×3 mL). The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, 30% EtOAc in hexane) to give **8a** (37.0 mg, 84%) as a yellow crystalline solid; mp 211–212 °C (CH_2Cl_2–hexane); R_f=0.61 (33% EtOAc in hexane); IR (KBr) 3322, 2923, 1298 cm^{-1}; ^1H NMR (300 MHz, acetone-d_6) δ 11.61 (br s, 1H), 8.51 (d, J=2.0 Hz, 1H), 8.12–8.06 (m, 3H), 7.88 (d, J=8.8 Hz, 1H), 7.70–7.63 (m, 2H), 7.61–7.54 (m, 1H), 7.25 (dd, J=2.0, 0.8 Hz, 1H); ^{13}C NMR (75 MHz, acetone-d_6) δ 144.0, 142.5, 135.5, 133.9, 131.0, 128.9 (×2), 128.6, 125.5 (×2), 119.9, 114.7, 107.5, 99.7; MS (+CI) m/z 239 ($M+H^+$, 100). Anal. Calcd for $C_{14}H_{10}N_2O_2$: C, 70.58; H, 4.23; N, 11.76. Found: C, 70.40; H, 4.11; N, 11.64%.

Other results are listed in Table 2.

4.8. Representative procedure for the Pd-catalyzed one-pot cross-coupling and heteroannulation toward nitroindoles

4.8.1. 6-Nitro-2-propylindole (8b). A mixture of **11b** (115.0 mg, 0.3 mmol), *n*-Bu_4NI (169.6 mg, 0.45 mmol), $Pd(PPh_3)_4$ (11.1 mg, 0.03 mmol), CuI (17.14 mg, 0.09 mmol), and 1-pentyne (40.8 mg, 60 μL, 0.6 mmol) in degassed DMF (5 mL) containing Et_3N (1 mL) was heated at ca. 80 °C for 21 h. After cooling to room temperature, the reaction mixture was diluted with EtOAc (20 mL) and washed with saturated aqueous NH_4Cl (10 mL) and brine (15 mL). The organic layer was dried over anhydrous $MgSO_4$, and evaporated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, MeOH–CH_2Cl_2–hexane=1:40:30) to give **8b** (51.7 mg, 84%, entry 7, Table 3) as a yellow crystalline solid;[30] mp 94–95 °C (CH_2Cl_2–hexane); R_f=0.54 (33% EtOAc in hexane); IR (film) 3367, 2962, 1302 cm^{-1}; ^1H NMR (300 MHz, acetone-d_6) δ 10.98 (br s, 1H), 8.42 (d, J=2.0 Hz, 1H), 8.04 (dd, J=8.8, 2.2 Hz, 1H), 7.73 (d, J=8.8 Hz, 1H), 6.55 (d, J=0.5 Hz, 1H), 2.98 (t, J=7.5 Hz, 2H), 1.94 (sextet, J=7.5 Hz, 2H), 1.13 (t, J=7.5 Hz, 3H); ^{13}C NMR (75 MHz, acetone-d_6) δ 141.5, 119.3, 118.6, 114.8, 114.0, 107.3, 106.7, 99.8, 29.9, 21.7, 12.8; MS (+CI) m/z 205 ($M+H^+$, 100). Anal. Calcd for $C_{11}H_{12}N_2O_2$: C, 64.69; H, 5.92; N, 13.72. Found: C, 64.74; H, 6.08; N, 14.13%.

Other results are summarized in Table 3.

4.8.2. 5-Nitro-2-phenylindole (7a). A yellow crystalline solid; mp 190–191 °C (CH_2Cl_2–hexane); R_f=0.37 (25% EtOAc in hexane); IR (film) 3344, 1329 cm^{-1}; ^1H NMR (300 MHz, acetone-d_6) δ 11.52 (br s, 1H), 8.69 (d, J=2.2 Hz, 1H), 8.26 (dd, J=8.9, 2.2 Hz, 1H), 8.05–8.00 (m, 2H), 7.76–7.60 (m, 3H), 7.56–7.50 (m, 1H), 7.28 (s, 1H); ^{13}C NMR (75 MHz, acetone-d_6) δ 141.3, 139.8, 130.9, 128.6 (×2), 128.2, 128.1, 128.0, 125.0 (×2), 116.6, 116.5, 110.8, 100.4; MS (+CI) m/z 239 ($M+H^+$, 100). Anal. Calcd for $C_{14}H_{10}N_2O_2$: C, 70.58; H, 4.23; N, 11.76. Found: C, 70.32; H, 4.11; N, 11.73%.

4.8.3. 5-Nitro-2-propylindole (7b). A yellow crystalline solid; mp 125–126 °C (CH_2Cl_2–hexane); R_f=0.34 (50% EtOAc in hexane); IR (KBr) 3325, 1314 cm^{-1}; ^1H NMR (300 MHz, acetone-d_6) δ 10.86 (br s, 1H), 8.57 (d, J=2.1 Hz, 1H), 8.11 (dd, J=9.0, 2.1 Hz, 1H), 7.58 (d, J=9.0 Hz, 1H), 6.56 (d, J=0.7 Hz, 1H), 2.92 (t, J=7.4 Hz, 2H), 1.90 (sextet, J=7.5 Hz, 2H), 1.12 (t, J=7.5 Hz, 3H); ^{13}C NMR (75 MHz, acetone-d_6) δ 143.6, 140.6, 138.9, 127.6, 115.4, 115.2, 109.8, 100.4, 28.1, 21.4, 12.5; MS (+CI) m/z 205 ($M+H^+$, 100). Anal. Calcd for $C_{11}H_{12}N_2O_2$: C, 64.69; H, 5.92; N, 13.72. Found: C, 64.74; H, 5.85; N, 13.46%.

4.8.4. 5-Nitro-2-(2′-hydroxyethyl)indole (7c). A crystalline solid; mp 114–115 °C (EtOAc–hexane); R_f=0.29 (67% EtOAc in hexane); IR (KBr) 3469, 3185 (br), 1512, 1471, 1337 cm^{-1}; ^1H NMR (300 MHz, acetone-d_6) δ 10.85 (br s, 1H), 8.60 (d, J=2.2 Hz, 1H), 8.11 (dd, J=9.0, 2.3 Hz, 1H), 7.75 (d, J=8.9 Hz, 1H), 6.67 (d, J=0.9 Hz, 1H), 4.22 (t, J=5.3 Hz, 1H), 4.07 (q, J=6.3 Hz, 2H), 3.18 (t, J=6.2 Hz, 2H); ^{13}C NMR (75 MHz, acetone-d_6) δ 142.0, 141.1, 139.3, 127.9, 115.8, 115.6, 110.5, 101.5, 60.8, 31.4; MS (+CI) m/z 207 ($M+H^+$, 100). Anal. Calcd for $C_{10}H_{10}N_2O_3$: C, 58.25; H, 4.89; N, 13.59. Found: C, 58.25; H, 5.00; N, 13.75%.

4.8.5. 5-Nitro-2-(3′-cyanopropyl)indole (7d). A crystalline solid; mp 125.5–126 °C (EtOAc–hexane); R_f=0.41 (50% EtOAc in hexane); IR (KBr) 3321, 2250, 1471, 1334 cm^{-1}; ^1H MNR (300 MHz, acetone-d_6): δ 10.9 (br s, 1H), 8.59 (d, J=2.1 Hz, 1H), 8.11 (dd, J=8.7, 2.4 Hz, 1H), 8.60 (d, J=8.7 Hz, 1H), 6.70 (s, 1H), 3.16 (t, J=7.5 Hz, 2H), 2.72 (t, J=7.2 Hz, 2H), 2.33–2.22 (m, 2H); ^{13}C NMR (75 MHz, acetone-d_6) δ 142.0, 141.5, 138.5, 128.1, 119.2, 116.1, 116.0, 110.6, 101.5, 26.7, 24.7, 15.8; MS (+CI) m/z 230 ($M+H^+$, 100). Anal. Calcd for $C_{12}H_{11}N_3O_2$: C, 62.87; H, 4.84; N, 18.33. Found: C, 62.75; H, 4.89; N, 18.37%.

4.8.6. 5-Nitro-2-(3′-chloropropyl)indole (7e). A crystalline solid; mp 107–107.5 °C (EtOAc–hexane); R_f=0.34 (25% EtOAc in hexane); IR (KBr): 3336, 1323 cm^{-1}; ^1H NMR (300 MHz, acetone-d_6) δ 10.86 (br s, 1H), 8.59 (d, J=1.8 Hz, 1H), 8.11 (dd, J=8.7, 2.1 Hz, 1H), 7.61 (d, J=

8.7 Hz, 1H), 6.68 (s, 1H), 3.84 (t, J=6.3 Hz, 2H), 3.17 (t, J=7.8 Hz, 2H), 2.44–2.35 (m, 2H); ^{13}C NMR (75 MHz, acetone-d_6) δ 142.2, 140.8, 139.2, 127.7, 115.7, 115.6, 110.2, 101.0, 43.2, 30.8, 24.2; MS (+CI) m/z 239 ($M+H^+$, 100). Anal. Calcd for $C_{11}H_{11}ClN_2O_2$: C, 55.36; H, 4.65; N, 11.74. Found: C, 55.28; H, 4.71; N, 11.76%.

4.8.7. 6-Nitro-2-(2′-hydroxyethyl)indole (8c). A crystalline solid; mp 141–142 °C (EtOAc–hexane); R_f=0.28 (50% EtOAc in hexane); IR (KBr) 3490, 3275 (br), 1501, 1316, 1051 cm^{-1}; ^{1}H NMR (300 MHz, acetone-d_6) δ 10.90 (br s, 1H), 8.47 (d, J=2.1 Hz, 1H), 8.03 (dd, J=8.4, 2.1 Hz, 1H), 7.73 (d, J=9.0 Hz, 1H), 6.60 (d, J=2.4 Hz, 1H), 4.25 (br s, 1H), 4.08 (br t, J=6.0 Hz, 2H), 3.21 (t, J=6.3 Hz, 2H); ^{13}C NMR (75 MHz, acetone-d_6) δ 145.3, 142.1, 134.2, 133.7, 118.8, 114.1, 107.2, 100.7, 60.7, 31.6; MS (+CI) m/z 207 ($M+H^+$, 100). Anal. Calcd for $C_{10}H_{10}N_2O_3$: C, 58.25; H, 4.89; N, 13.59. Found: C, 58.29; H, 4.77; N, 13.37%.

4.8.8. 6-Nitro-2-(3′-cyanopropyl)indole (8d). A crystalline solid; mp 117–118 °C (EtOAc–hexane); R_f=0.47 (50% EtOAc in hexane); IR (KBr) 3326, 2254, 1499, 1308 cm^{-1}; ^{1}H NMR (300 MHz, acetone-d_6) δ 10.99 (br s, 1H), 8.41 (d, J=1.8 Hz, 1H), 8.18 (dd, J=8.7, 2.4 Hz, 1H), 7.75 (d, J=8.7 Hz, 1H), 6.63 (d, J=3.0 Hz, 1H), 3.19 (t, J=7.8 Hz, 2H), 2.72 (t, J=8.4 Hz, 2H), 2.35–2.27 (m, 2H); ^{13}C NMR (75 MHz, acetone-d_6) δ 145.9, 142.8, 134.6, 133.6, 131.6, 119.1, 114.3, 107.1, 100.6, 26.9, 24.7, 15.9; MS (+CI) m/z 230 ($M+H^+$, 100). Anal. Calcd for $C_{12}H_{11}N_3O_2$: C, 62.87; H, 4.84; N, 18.33. Found: C, 62.72; H, 4.85; N, 18.46%.

4.8.9. 6-Nitro-2-(3′-chloropropyl)indole (8e). A white crystalline solid; mp 98–99 °C (EtOAc–hexane); R_f=0.49 (25% EtOAc in hexane); IR (KBr) 3329, 1505, 1337, 1298 cm^{-1}; ^{1}H NMR (300 MHz, acetone-d_6) δ 10.95 (br s, 1H), 8.42 (d, J=1.2 Hz, 1H), 8.04 (dd, J=8.7, 2.1 Hz, 1H), 7.74 (d, J=8.7 Hz, 1H), 6.60 (d, J=3.0 Hz, 1H), 3.83 (t, J=6.6 Hz, 2H), 3.19 (t, J=7.8 Hz, 2H), 2.45–2.35 (m, 2H); ^{13}C NMR (75 MHz, acetone-d_6) δ 145.7, 142.0, 134.6, 133.7, 118.1, 114.3, 107.1, 100.4, 44.0, 31.6, 25.2; MS (+CI) m/z 239 ($M+H^+$, 100). Anal. Calcd for $C_{11}H_{11}ClN_2O_2$: C, 55.36; H, 4.65; N, 11.74. Found: C, 55.28; H, 4.51; N, 11.72%.

4.8.10. 7-Nitro-2-phenylindole (9a). A white crystalline solid; mp 142–143 °C (CH_2Cl_2–hexane); R_f=0.74 (25% EtOAc in hexane); IR (film) 3149, 2921, 1338, 1292 cm^{-1}; ^{1}H NMR (300 MHz, acetone-d_6) δ 11.09 (br s, 1H), 8.25 (dd, J=8.1, 0.9 Hz, 1H), 8.18 (dd, J=8.1, 0.9 Hz, 1H), 8.13–8.09 (m, 2H), 7.67–7.55 (m, 3H), 7.40 (t, J=7.9 Hz, 1H), 7.25 (d, J=1.6 Hz, 1H); ^{13}C NMR (75 MHz, acetone-d_6) δ 140.8, 132.9, 130.8, 129.8, 128.9, 128.6 (×2), 128.2, 128.0, 125.8 (×2), 119.1, 118.3, 100.4; MS (+CI) m/z 239 ($M+H^+$, 44), 153 (100). Anal. Calcd for $C_{14}H_{10}N_2O_2$: C, 70.58; H, 4.23; N, 11.76. Found: C, 70.36; H, 4.25; N, 12.00%.

4.8.11. 7-Nitro-2-propylindole (9b). A yellow crystalline solid; mp 79–80 °C (CH_2Cl_2–hexane); R_f=0.71 (25% EtOAc in hexane); IR (KBr) 3409, 2956, 1512, 1339 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.69 (br s, 1H), 8.05 (d, J=8.1 Hz, 1H), 7.80 (d, J=7.6 Hz, 1H), 7.13 (t, J=7.9 Hz, 1H), 6.38 (s, 1H), 2.81 (t, J=7.4 Hz, 2H), 1.80 (sextet, J=7.4 Hz, 2H), 1.04 (t, J=7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.7, 132.6, 129.4, 128.4, 127.6, 118.9, 117.9, 100.7, 30.0, 22.2, 13.8; MS (+CI) m/z 205 ($M+H^+$, 100). Anal. Calcd for $C_{11}H_{12}N_2O_2$: C, 64.69; H, 5.92; N, 13.72. Found: C, 64.90; H, 6.11; N, 13.75%.

4.8.12. 7-Nitro-2-(2′-hydroxyethyl)indole (9c). A yellow crystalline solid; mp 117–118 °C (EtOAc–hexane); R_f=0.47 (50% EtOAc in hexane); IR (KBr): 3394, 3291 (br), 2923, 1514, 1338 cm^{-1}; ^{1}H NMR (300 MHz, acetone-d_6) δ 11.11 (br s, 1H), 8.19 (d, J=7.8 Hz, 1H), 8.09 (d, J=7.8 Hz, 1H), 7.34 (t, J=7.8 Hz, 1H), 6.67 (d, J=0.9 Hz, 1H), 4.29 (br s, 1H), 4.11 (t, J=6.2 Hz, 2H), 3.26 (t, J=6.4 Hz, 2H); ^{13}C NMR (75 MHz, acetone-d_6) δ 141.7, 132.8, 132.2, 129.1, 127.4, 118.5, 117.2, 101.0, 61.0, 31.0; MS (+CI) m/z 207 ($M+H^+$, 100). Anal. Calcd for $C_{10}H_{10}N_2O_3$: C, 58.25; H, 4.89; N, 13.59. Found: C, 58.39; H, 4.89; N, 13.70%.

Acknowledgements

This work is supported in part by the Innovation and Technology Fund (ITS/119/00) from the Innovation and Technology Commission of the Hong Kong Special Administration Region, China, the Department of Chemistry, HKUST, and a research grant provided by Zhejiang University. Elemental analyses performed by Zhejiang University are acknowledged. W. -M. Dai is the recipient of Cheung Kong Scholars Award of The Ministry of Education of China.

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