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Barium manganate in microwave-assisted oxidation reactions: synthesis of solvatochromic 2,4,6-triarylpyrimidines

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ABSTRACT

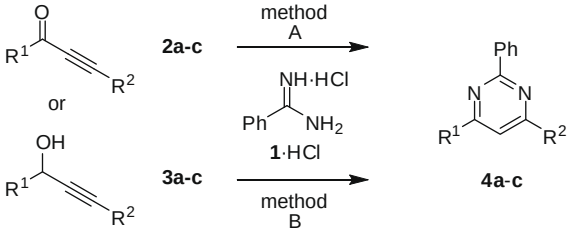
Synthesis of 2,4,6-trisubstituted pyrimidines by tandem oxidation/heterocyclocondensation of propargylic alcohols and amidines is effected rapidly and efficiently under microwave dielectric heating using barium manganate as oxidant. Irradiation at 150 °C in ethanol–acetic acid for 45 min results in dramatic improvements in yield over the corresponding manganese dioxide-mediated method and establishes a rapid route to triarylpyrimidines in order to investigate their photophysical properties.

Efficient synthetic routes to functionalised chromophoric compounds possessing tunable absorption and emission properties are essential in the search for materials for optoelectronic devices, light-energy harvesting and fluorescence imaging microscopy.[1] Synthetic[2] and theoretical[3] studies have shown that unusual electrochromic, photochromic, luminescent or nonlinear optical properties can be developed by incorporating aromatic and heteroaromatic groups with different electronic properties onto a chromophoric interlink within a donor–acceptor (D–A) molecular framework.[4–6] The use of a pyrimidine scaffold in this regard has received very little attention, until recently when the fluorescence properties of π-extended pyrimidine systems was recognised.[7] As part of our interest in the synthesis of heterocycles with readily-modulated photophysical properties,[8] we rationalised that the tandem oxidation/heterocyclocondensation of propargylic alcohols and amidines under microwave irradiation would enable a rapid route to a library of π-extended pyrimidines that could incorporate a range of donor and acceptor groups in order to tune their photophysical behaviour.

Microwave dielectric heating has received increasing attention in recent years as a valuable alternative to the use of conductive heating for accelerating transformations, both in synthetic chemistry and the biosciences.[9] Our own studies have demonstrated that microwave irradiation provides a rapid and convenient alternative to conductive heating methods for the cyclocondensation of amidines and ethynyl ketones to give disubstituted pyrimidines in good yield.[10] Despite this good precedent, there were a number of concerns prior to the outset of a microwave-mediated approach to this pyrimidine library: our previously established method had been found to be less efficient both for the synthesis of trisubstituted pyrimidines[10] and when using electron-rich 1,3-diarylpropynone precursors,[11] which threatened the scope of any photophysical review. Furthermore, when considering a tandem oxidation–heterocyclocondensation route, only a very limited range of pyrimidines had been prepared before by this methodology.[12]

These concerns were indeed found to be well-justified upon investigation. Synthesis of 2,4-diphenylpyrimidine (**4a**) by cyclocondensation of benzamidine **1** and propynone **2a**, either used directly or produced in situ by tandem oxidation of propargylic alcohol **3a** with MnO_2, was highly efficient under microwave irradiation, whereas the corresponding process for the synthesis of 2-phenyl-4,6-bis(4-methoxyphenyl)pyrimidine (**4b**) was less efficient (Scheme 1, Table 1). The tandem oxidation–heterocyclocondensation of amidine **1** and an even more electron-rich propargylic alcohol **3c** with MnO_2 under microwave irradiation barely gave any yield of pyrimidine **4c** at all. It was concluded that a new or refined method was required in order to access a library of 2,4,6-triarylpyrimidines with different D–A properties for photophysical study.

It has been shown that barium manganate is a useful reagent for the oxidation of benzylic, allylic and propargylic alcohols[13,14] and, when used in a tandem oxidation/Wittig reaction,[15] was efficient



Scheme 1. Method A[10,11] (cyclocondensation): Na_2CO_3, MeCN, μω, 120 °C, 40 min; method B[12] (tandem oxidation): MnO_2, Na_2CO_3, MeCN, μω, 150 °C, 45–60 min. – = not determined; μω denotes microwaves.

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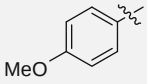
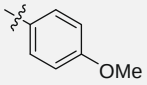
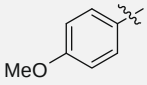
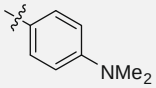
Table 1
Isolated yield (%) of **4a–c** using method A or B

	R^1	R^2	A	B
a		H	98	84
b			41	52
c			—	19

and gave higher yields than manganese dioxide.[16] Following our previous observation that a related tandem oxidation/heteroannulation process was more facile under microwave irradiation with $BaMnO_4$ than with MnO_2, due to its more efficient coupling with the rapidly oscillating electric field,[17] the use of this oxidant (3 equiv) was investigated in the microwave-assisted tandem oxidation/heterocyclocondensation of propargylic alcohol **3a** (1 equiv) and benzamidine **1** (1 equiv). It was thought that this would be a good substrate to study, as the heterocyclisation was highly efficient (Table 1). Under the conditions investigated (Table 2), the use of $BaMnO_4$ in this tandem process gave pyrimidine **4a** in good yield, with microwave irradiation at 150 °C in a mixture of EtOH–acetic acid for 45 min appearing to be optimum (entry 8).

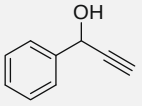
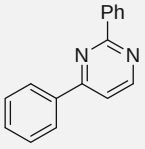
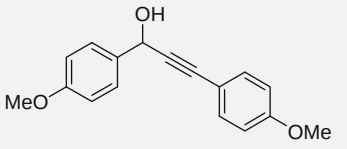
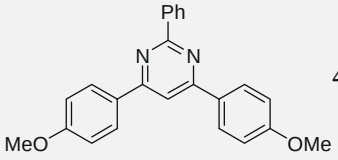
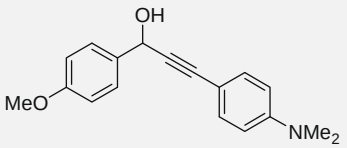
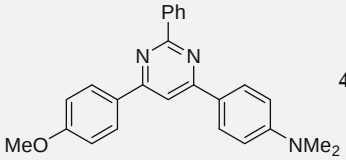
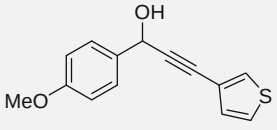
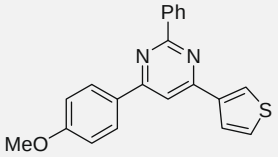
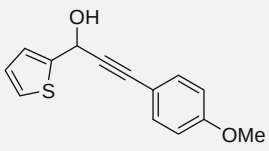
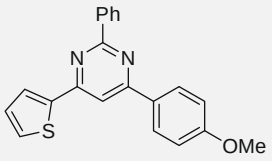
Table 2
Optimising the microwave-assisted synthesis of pyrimidine **4a**

Entry	Reagents and conditions[a]	Yield[b]
1	MnO_2, μω, 140–150 °C,[c] MeCN, 45 min	85
2	$BaMnO_4$, μω, 150 °C, MeCN, 45 min	88
3[d]	MnO_2, MeCN, reflux, 10 h	72
4[d]	$BaMnO_4$, MeCN, reflux, 10 h	76
5	$BaMnO_4$, μω, 150 °C, MeOH, 45 min	50
6	$BaMnO_4$, μω, 150 °C, EtOH, 45 min	62
7	$BaMnO_4$, μω, 120 °C, EtOH–AcOH, 45 min	82
8	**$BaMnO_4$, μω, 150 °C, EtOH–AcOH, 45 min**	**92**
9	$BaMnO_4$, μω, 170 °C, EtOH–AcOH, 45 min	86
10	$BaMnO_4$, μω, 150 °C, EtOH–AcOH, 30 min	64
11	$BaMnO_4$, μω, 150 °C, EtOH–AcOH, 60 min	90

[a] μω denotes experiments were conducted under microwave irradiation in a 10 mL Pyrex vessel using a single mode CEM Discover® microwave synthesiser at the given temperature through moderation of the initial microwave power (150 W), unless noted otherwise. The optimum conditions are indicated in bold.
[b] Yield refers to the percentage isolated yield after purification by column chromatography on silica gel.
[c] Although the temperature was set to 150 °C, the actual temperature of reaction was considerably lower due to inefficient coupling with the microwave irradiation.
[d] Carried out by traditional conductive heating using an oil bath.

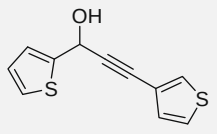
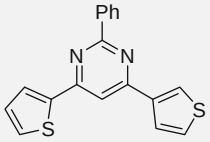
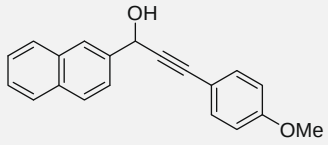
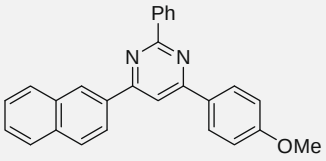
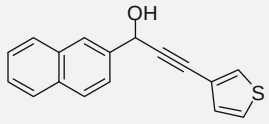
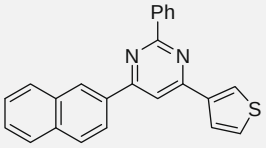
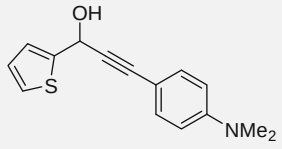
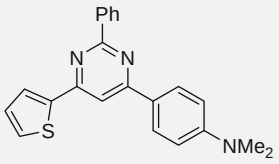
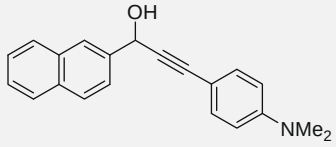
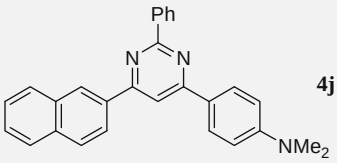
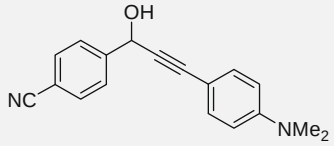
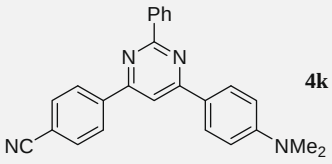
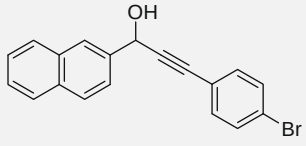
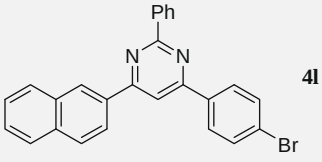
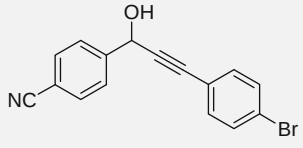
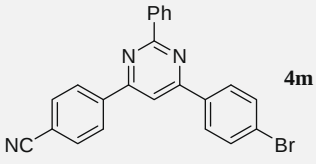
These refined conditions (Method 1)[18] were tested using a range of propargylic alcohols **3** (Table 3), prepared according to the method of Tykwinski.[14] The isolated yield of the pyrimidine product was compared with two other procedures: microwave irradiation in MeCN using MnO_2 as oxidant (Method 2) and an existing traditional method of pyrimidine formation under conductive heating by cyclocondensation of amidine **1** and the corre-

Table 3
Scope of the microwave-assisted tandem oxidation/heterocyclocondensation using $BaMnO_4$

Entry	Alcohol **3**	Pyrimidine **4**	Yield%[a] Method 1[b]	Yield%[a] Method 2[c]	Yield%[a] Method 3[d]
1	 **3a**	 **4a**	92	85	0[e]
2	 **3b**	 **4b**	72	42	30
3	 **3c**	 **4c**	72	19[f]	24
4	 **3d**	 **4d**	79	10[f]	11
5	 **3e**	 **4e**	82	32	29

(*continued on next page*)

Table 3 (*continued*)

Entry	Alcohol **3**	Pyrimidine **4**	Yield%[a] Method 1[b]	Yield%[a] Method 2[c]	Yield%[a] Method 3[d]
6	 **3f**	 **4f**	86	44	40
7	 **3g**	 **4g**	73[g]	48	31
8	 **3h**	 **4h**	68	36	24
9	 **3i**	 **4i**	68	–	0[e]
10	 **3j**	 **4j**	74	–	36
11	 **3k**	 **4k**	62	–	0[e]
12	 **3l**	 **4l**	80	–	40
13	 **3m**	 **4m**	76	–	22

[a] Isolated yield of pyrimidine **4** after purification by column chromatography on silica gel.

[b] Method 1 (method of choice): microwave irradiation of benzamidine **1** (1 equiv) and propargylic alcohol **3** (1 equiv) at 150 °C using $BaMnO_4$ (3 equiv) in EtOH–AcOH in a sealed tube for 45 min using a CEM Discover® microwave synthesiser by moderating the initial microwave power (150 W).

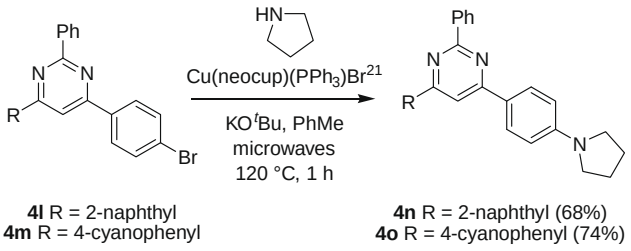
[c] Method 2 (for comparison): microwave irradiation of benzamidine **1** (1 equiv) and propargylic alcohol **3** (1 equiv) at 150 °C (set temperature; actual temperature may be 135–150 °C; see Ref. [17] for details) using MnO_2 (3 equiv) in MeCN in a sealed tube for 45 min using a CEM Discover® microwave synthesiser by moderating the initial microwave power (150 W). — = not determined.

[d] Method 3 (for comparison): conductive heating of benzamidine **1** (1 equiv) and the corresponding chalcone (1 equiv) at reflux in EtOH in the presence of NaOH, moisture and air for 10 h, according to the method of Dodson and Seyler.[19]

[e] The reaction failed to give any of the desired pyrimidine product **4**.

[f] Reaction time was extended to 1 h.

[g] No purification by column chromatography was required.



4l R = 2-naphthyl
4m R = 4-cyanophenyl

4n R = 2-naphthyl (68%)
4o R = 4-cyanophenyl (74%)

Scheme 2. Further library diversification by copper-mediated N-arylation.

sponding chalcone (Method 3), according to the method of Dodson and Seyler,[19] for select cases. It was gratifying to observe that a tandem oxidation/heterocyclocondensation reaction offered a viable route to a range of π-extended pyrimidines. Furthermore, in all cases, the refined conditions using $BaMnO_4$ gave significant improvements in yield over the other methods making it by far the more efficient procedure.

In order to broaden the electronic profile of the π-extended pyrimidines accesible by this methodology, bromides **4l,m** were transformed by copper-mediated N-arylation[20] using the preformed Cu(I) catalyst Cu(neocup)(PPh_3)Br.[21] The original conductive heating procedure was modified[22] and carried out in the presence of pyrrolidine and potassium *tert*-butoxide at 120 °C for one hour in toluene under microwave irradiation[23] to give pyrrolidino-derivatives **4n,o**, respectively, in good yield (Scheme 2).

The photophysical properties of a selection of the functionalised pyrimidines were assessed.[24] The pyrimidine species displayed solution-state ($CHCl_3$) fluorescence at room temperature: each possessed a single broad emission in the visible region following excitation at 360 nm. The short (<10 ns) emission lifetimes (mono-exponential, consistent with a single decaying excited state) were also characteristic of a fluorescence in each case. With the exception of **4a**, notable Stokes shifts were attributed to the presence of the donor and acceptor groups, which are likely to induce significant charge transfer character to the excited state. Consequently, the origin of the fluorescence in **4a** is more likely to be a locally excited singlet $\pi \leftarrow \pi^*$ transition. The most significant red-shifts in both λ_{abs} and λ_{em} were achieved with a naphthyl unit as the acceptor component. Therefore the charge transfer character was confirmed by assessing the solvent dependence of the emission from **4j** in cyclohexane, chloroform and DMSO (Table 4). The steady state emission spectra showed that the fluorescence band red-shifts significantly with a concomitant broadening as solvent polarity increases, together with a corresponding reduction in quantum yield. The corresponding excitation spectra also revealed a low-energy broadening of the lowest energy band (360–400 nm), which correlate with the observations from the absorption spectra. An additional example is shown graphically in Figure 1 again showing the significant low-energy shift in emission maximum

Table 4
Solution state photophysical properties of some selected pyrimidines

Compound	λ_{abs} (log ε)/nm	λ_{em}/nm	τ/ns	ϕ_{fl}
4a[a]	278 (4.26)	311	0.6	0.51
4c[a]	365 (4.54)	453	7.1	0.49
4i[a]	371 (4.64)	473	7.0	0.46
4j[a]	379 (4.84)	510	2.4	0.40
4j[b]	368 (4.68)	422	2.9	0.48
4j[c]	382 (4.92)	599	1.6	0.22
4k[a]	376 (4.82)	495	3.5	0.44
4n[a]	430 (4.40)	498	2.4	0.19
4o[a]	385 (4.38)	518	3.3	0.23

[a] In chloroform.
[b] In cyclohexane.
[c] In dimethylsulfoxide.

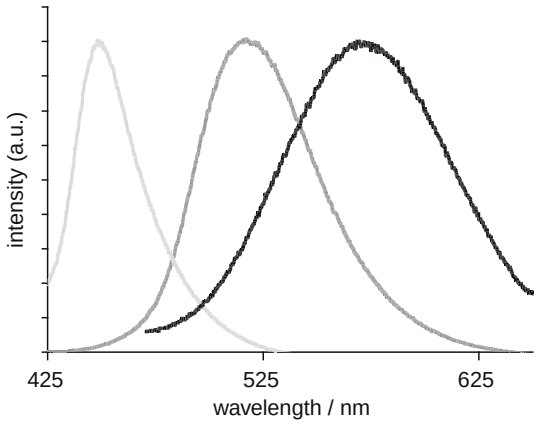


Figure 1. Normalised emission (λ_{ex} = 370 nm) spectra showing the solvent dependence of compound **4n** (black: DMSO; grey: $CHCl_3$; light grey: cyclohexane).

for **4n** upon increasing solvent polarity. Taken together these results suggest that the room temperature visible fluorescence from the donor–acceptor appended pyrimidine species is due to intramolecular CT, and is in agreement with a recent report into oligomeric pyrimidine species[25] and other related species.[7] These results are also consistent with our previous findings on related donor–acceptor frameworks based upon cyanopyridines,[8] which also show pronounced solvatochromic behaviour from an emitting CT-excited state.

In conclusion, tandem oxidation/heterocyclocondensation of a propargylic alcohol and benzamidine using $BaMnO_4$ under microwave irradiation provides a rapid route to pyrimidines, which can be further derivatised by microwave-assisted copper-mediated N-arylation. The π-extended pyrimidines so-formed by this approach are highly fluorescent in the visible region, displaying solvent-dependent emission wavelengths suggestive of charge transfer-dominated excited states.

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References and notes

1. (a) Kanis, D. R.; Ratner, M. A.; Marks, T. J. *Chem. Rev.* **1994**, *94*, 195; (b) Raposo, M. M. M.; Sousa, A. M. R. C.; Kirsch, G.; Cardoso, P.; Belsley, M.; Gomes, E. D.-M.; Fonseca, A. M. C. *Org. Lett.* **2006**, *8*, 3681.
2. (a) Rao, V. P.; Jen, A. K.-Y.; Wong, K. Y.; Drost, K. J. *Tetrahedron Lett.* **1993**, *34*, 1747; (b) Jen, A. K.-Y.; Wong, K. Y.; Drost, K. J. *Chem. Commun.* **1993**, 90.
3. (a) Varanasi, P. R.; Jen, A. K.-Y.; Chandrasekhar, J.; Namboothiri, N. N. I.; Rathna, A. *J. Am. Chem. Soc.* **1996**, *118*, 12443; (b) Albert, I. D. L.; Marks, T. J.; Ratner, M. A. *J. Am. Chem. Soc.* **1997**, *119*, 6575.
4. (a) Rao, V. P.; Jen, A. K.-Y.; Caldwell, J. B. *Tetrahedron Lett.* **1994**, *35*, 3849; (b) Facchetti, A.; Beverina, L.; Van-der Boom, M. E.; Dutta, E. G.; Pagani, G. A.; Marks, T. J. *J. Am. Chem. Soc.* **2006**, *128*, 2142 and references cited therein.
5. Grabowski, Z. R.; Rotkiewicz, K.; Rettig, W. *Chem. Rev.* **2003**, *103*, 3899.
6. Thompson, B. C.; About, K. A.; Reynolds, J. R.; Nakatani, K.; Audebert, P. *New J. Chem.* **2005**, *29*, 1128.
7. Itami, K.; Yamazaki, D.; Yoshida, J.-i. *J. Am. Chem. Soc.* **2004**, *126*, 15396.
8. Bagley, M. C.; Lin, Z.; Pope, S. J. A. *Chem. Commun.* **2009**, 5165.
9. (a) Caddick, S.; Fitzmaurice, R. *Tetrahedron* **2009**, *65*, 3325; (b) Kappe, C. O. *Chem. Soc. Rev.* **2008**, *37*, 1127; (c) Collins, J. M.; Leadbeater, N. E. *Org. Biomol. Chem.* **2007**, *5*, 1141; (d) Adam, D. *Nature* **2003**, *421*, 571; (e)*Microwaves in Organic Synthesis*; Loupy, A., Ed.; Wiley-VCH: Weinheim, 2002; (f) Kappe, C. O. *Angew. Chem., Int. Ed.* **2004**, *43*, 6250; (g) Hayes, B. L. *Aldrichim. Acta* **2004**, *37*, 66; (h) Kuhnert, N. *Angew. Chem., Int. Ed.* **2002**, *41*, 1863; (i) Lidström, P.; Tierney, J.; Wathey, B.; Westman, J. *Tetrahedron* **2001**, *57*, 9225; (j) Loupy, A.; Petit, A.; Hamelin, J.; Texier-Boullet, F.; Jacquault, P.; Mathé, D. *Synthesis* **1998**, 1213; (k) Gabriel, C.; Gabriel, S.; Grant, E. H.; Halstead, B. S. J.; Mingos, D. M. P. *Chem. Soc. Rev.* **1998**, *27*, 213; (l) Galema, S. A. *Chem. Soc. Rev.* **1997**, *26*, 233; (m) Caddick, S. *Tetrahedron* **1995**, *51*, 10403; (n) Strauss, C. R.; Trainor, R. W. *Aust. J. Chem.* **1995**, *48*, 1665.
10. Bagley, M. C.; Hughes, D. D.; Taylor, P. H. *Synlett* **2003**, 259.

11. Bagley, M. C.; Hughes, D. D.; Lubinu, M. C.; Merritt, E. A.; Taylor, P. H.; Tomkinson, N. C. O. *QSAR Comb. Sci.* **2004**, *23*, 859.
12. Bagley, M. C.; Hughes, D. D.; Sabo, H. M.; Taylor, P. H.; Xiong, X. *Synlett* **2003**, 1443.
13. (a) Firouzabadi, H.; Karimi, B.; Abbassi, M. *J. Chem. Res.* **1999**, 236; (b) Kim, K. S.; Chung, S.; Cho, I. H.; Hahn, C. S. *Tetrahedron Lett.* **1989**, *30*, 2559; (c) Firouzabadi, H.; Ghaderi, E. *Tetrahedron Lett.* **1978**, 839; (d) Fatiadi, A. J. *Synthesis* **1987**, 85.
14. Shi Shun, A.; Chernick, E.; Eisler, S.; Tykwinski, R. *J. Org. Chem.* **2003**, *68*, 1339.
15. For reports on MnO_2-mediated tandem oxidation/Wittig reactions and related methodology, see: (a) Lang, S.; Taylor, R. J. K. *Tetrahedron Lett.* **2006**, *47*, 5489; (b) Phillips, D. J.; Pillinger, K. S.; Li, W.; Taylor, A. E.; Graham, A. E. *Chem. Commun.* **2006**, 2280; (c) Wilfred, C.; Taylor, R. J. K.; Wilfred, C.; Taylor, R. J. K. *Synth. Commun.* **2005**, *35*, 2859; (d) Raw, S. A.; Reid, M.; Roman, E.; Taylor, R. J. K. *Synlett* **2004**, 819; (e) Aitken, D. J.; Faure, S.; Roche, S. *Tetrahedron Lett.* **2003**, *44*, 8827; (f) Foot, J. S.; Kanno, H.; Giblin, G. M. P.; Taylor, R. J. K. *Synthesis* **2003**, 1055; (g) Blackburn, L.; Kanno, H.; Taylor, R. J. K. *Tetrahedron Lett.* **2003**, *44*, 115; (h) Runcie, K. A.; Taylor, R. J. K. *Chem. Commun.* **2002**, 974; (i) Blackburn, L.; Pei, C.; Taylor, R. J. K. *Synlett* **2002**, 215; (j) Blackburn, L.; Taylor, R. J. K. *Org. Lett.* **2001**, *3*, 1637; (k) Wei, X.; Taylor, R. J. K. *J. Org. Chem.* **2000**, *65*, 617; (l) Blackburn, L.; Wei, X.; Taylor, R. J. K. *Chem. Commun.* **1999**, 1337; (m) Wei, X.; Taylor, R. J. K. *Tetrahedron Lett.* **1998**, *39*, 3815.
16. Shuto, S.; Niizuma, S.; Matsuda, A. *J. Org. Chem.* **1998**, *63*, 4489.
17. See preceding manuscript. Barium manganate in microwave-assisted oxidation reactions: synthesis of lactones by oxidative cyclization of diols. Bagley, M. C.; Lin, Z.; Phillips, D. J.; Graham, A. E. *Tetrahedron Lett.* **2009**, *50*, 6823.
18. In a typical procedure for the microwave-assisted in situ tandem oxidation-heteroannulation reaction mediated by $BaMnO_4$, a mixture of benzamidine (**1**) (0.57 mmol, 1 equiv), 1-(4-cyanophenyl)-3-[4-bromophenyl]prop-2-yn-1-ol (**3m**) (0.57 mmol, 1 equiv) and barium manganate (1.70 mmol, 3 equiv) in EtOH–AcOH (5:1) (5 mL) was irradiated at 150 °C in a sealed pressure-rated reaction tube (10 mL), at an initial power of 150 W, for 45 min in a self-turned single mode CEM Discover® Focused Synthesiser. The mixture was cooled rapidly to room temperature, by passing compressed air through the microwave cavity for 5 min, and then filtered through Celite. The filtrate was poured into water (15 mL) and extracted with EtOAc (8 mL). The aqueous layer was further extracted with EtOAc (8 mL) and the organic extracts were combined, washed sequentially with saturated aqueous sodium hydrogen carbonate (10 mL) and brine (10 mL), dried (Na_2SO_4) and evaporated *in* vacuo. Purification by column chromatography on silica gel, eluting with EtOAc–petroleum ether (1:6 v/v), gave 4-[6-(4-bromophenyl)-2-phenylpyrimidin-4-yl]benzonitrile (**4m**) (0.18 g, 76%) as colourless crystals, mp 231–232 °C (found: $M^{\cdot+}$, 411.0356. $C_{23}H_{14}{}^{79}BrN_3$ [*M*] requires 411.0371); IR (KBr) ν_{max} 2919, 2849, 2224, 1592, 1572, 1525, 1363; ^1H NMR (400 MHz, $CDCl_3$) δ 8.71 (2H, m, 2,6-*Ph*H), 8.41 (2H, d, *J* 8.8, 3′,5′-H), 8.19 (2H, d, *J* 8.8, 3″,5″-H), 8.01 (1H, s, 5-H), 7.88 (2H, d, *J* 8.8, 2′,6′-H), 7.73 (2H, d, *J* 8.8, 2″,6″-H), 7.56 (3H, m, *Ph*H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 165.1 (C), 163.2 (C), 162.8 (C), 142.4 (C), 138.2 (C), 137.4 (C), 136.4 (C), 133.1 (CH), 132.0 (CH), 131.6 (CH), 131.4 (CH), 129.6 (CH), 128.9 (CH), 127.8 (CH), 126.0 (C), 114.0 (CN), 110.6 (CH); MS (EI) *m/z* (rel. intensity) 413 ($M[^{81}Br]^{\cdot+}$, 97%), 411 ($M[^{79}Br]^{\cdot+}$, 100).
19. Dodson, R.; Seyler, J. *J. Org. Chem.* **1951**, *16*, 461.
20. Venkataraman, D.; Gujadhur, R. K.; Kintigh, J. T. *Tetrahedron Lett.* **2001**, *42*, 4791.
21. Venkataraman, D.; Gujadhur, R. K.; Bates, C. G. *Org. Lett.* **2001**, *3*, 4315.
22. In a typical procedure for the microwave-assisted Cu-mediated N-arylation, a solution of benzonitrile **4m** (0.57 mmol, 1 equiv) in toluene (3 mL) was added to a stirred solution of pyrrolidine (1.13 mmol, 2 equiv), Cu(neocup)(PPh_3)Br[21] (10 mol %) and potassium *tert*-butoxide (0.85 mmol, 1.5 equiv) in toluene (3 mL) in a pressure-rated Pyrex reaction tube (10 mL). The vessel was sealed and irradiated at 120 °C, at an initial power of 150 W, in a self-turned single mode CEM Discover® Focused Synthesiser for 1 h. The mixture was then cooled rapidly to room temperature, by passing compressed air through the microwave cavity for 5 min, and then filtered through Celite. The filtrate was poured into water (15 mL) and extracted with Et_2O (15 mL). The aqueous layer was further extracted with Et_2O (15 mL) and the organic extracts were combined, dried (Na_2SO_4) and evaporated in vacuo. Purification by column chromatography on silica gel, eluting with EtOAc–petroleum ether (1:6 v/v), gave 4-{2-phenyl-6-[4-(pyrrolidin-1-yl)phenyl]pyrimidin-4-yl}benzonitrile (**4o**) (0.17 g, 74%) as orange crystals, mp 227–228 °C, with satisfactory spectroscopic and spectrometric characterisation data.
23. For related CuI-mediated microwave-assisted procedures for Ullmann-condensation, see: Bagley, M. C.; Dix, M. C.; Fusillo, V. *Tetrahedron Lett.* **2009**, *50*, 3661 and references cited therein.
24. Steady state spectra were recorded using a Perkin–Elmer LS55. Luminescence lifetimes were obtained on a JobinYvon-Horiba Fluorolog spectrometer fitted with a JY TBX picosecond photodetection module with a pulsed source 372 nm NanoLED (operating at 1 MHz). All lifetimes were obtained using the JY-Horiba FluorHub single photon-counting module.
25. Achelle, S.; Nouira, I.; Pfaffinger, B.; Ramondenc, Y.; Ple, N.; Rodriguez-Lopez, J. *J. Org. Chem.* **2009**, *74*, 3711.