A selective synthesis of 4-bromoisoquinoline and 4-bromoisquinolone

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2-Alkynyl benzyl azides smoothly underwent an electrocyclic reaction catalysed by palladium to selectively afford either 4-bromoisoquinoline and 4-bromoisquinolones under different conditions. 4-Bromoisoquinoline was synthesised in the presence of $PdBr_2/CuBr_2/LiBr$ in MeCN, and 4-bromoisoquinolone was selectively produced with $PdBr_2/CuBr_2/HOAc$ in CH_2ClCH_2Cl. A bromine was introduced into the products which makes the methodology more attractive for organic synthesis.

Keywords: 2-alkynyl benzyl azides, selectivity, cyclisation, isoquinoline, isoquinolone

Isoquinolines[1–3] and isoquinolin-1(2*H*)-ones[4–7] are found in many natural products and synthetic pharmaceuticals and a number of efficient and selective methods have been developed for their synthesis.[8–13] Although the classical routes to isoquinolines involve the Bischler-Napieralski[14] or Pictet-Spengler reaction,[15] these approaches often have drawbacks, for example, the use of strong acids and elevated temperature,[16] which are not suitable for sensitive substrates. This has led to the development of new methodology. In recent years, new transition metal catalysed reactions have been developed for the synthesis of substituted isoquinolines from phenylacetylene substrates.[17–24] These reactions have proved to be extremely efficient in the synthesis of a wide variety of 3,4-substituted isoquinolines.

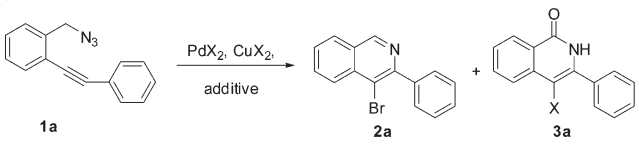
There are also a number of approaches to the synthesis of isoquinolin-1(2*H*)-ones reported in the literature,[25–29] but most of them suffer from a poor precursor scope and less structural diversity. Recently, the transition metal catalysed synthesis of substituted isoquinolin-1(2*H*)-one derivatives has received attention, for example, Pd-catalysed multicomponent synthesis of oxazoline and benzoxazole,[30] Pd-catalysed synthesis of 4-aminophthalazin-1(2*H*)-one,[31] and synthesis of quinazolino-[3,2-a]-quinazolines via a palladium-catalysed three-component reaction.[32]

We recently reported the first successful application of the halopalladation cyclisation of alkynes with azides to the synthesis of 4-haloisoquinolines and 3-haloindoles.[33] As part of our continuing studies on the efficient preparation of biologically important heterocycles,[34] we describe herein strategies for the synthesis of 4-bromoisoquinolines and 4-bromoisoquinolin-1(2*H*)-one via a reagent-based cyclisation of 2-alkynyl benzyl azides (Scheme 1). To the best of our knowledge, there are no reports of an efficient synthesis of 4-bromoisoquinolines and 4-bromoisoquinolin-1(2*H*)-one using these intermediates.

In our earlier studies with 2-phenylethynyl benzyl azide (**1a**), we have devised route for the preparation of bromoisoquinolines in the presence of 5 mol% of $PdBr_2$, 3 equiv. of $CuBr_2$, and 2 equiv. of LiBr as additive in MeCN.[33] As shown in Table 1, exploratory experiments revealed that treatment of 2-phenylethynyl benzyl azide with $PdBr_2/CuBr_2/LiBr$ in CH_2ClCH_2Cl was unsuccessful for the bromopalladation annulation of **1a** to afford product 4-bromo-3-phenylisoquinoline (**2a**). However, unexpectedly 4-bromo-3-phenylisoquinolin-1(2*H*)-one (**3a**) was isolated (entry 2). During the course of our investigation, we observed that an identical yield of **3a** was obtained by further decreasing the additive loadings of LiBr to 0.2 equiv, coupled with a decrease in the yield of **2a** (entries 3 and 4). Encouraged by these results, we decided to focus on the development of appropriate protocols for reagent-based synthesis of 4-bromoisoquinolines and 4-bromoisoquinolin-1(2*H*)-one. The effect of additive on the reaction was examined, employing 5 mol% of $PdBr_2$ and 3 equiv. of $CuBr_2$ in CH_2ClCH_2Cl (entries 5–8). After a series of trials, 2 equiv. of LiBr as additive and MeCN as solvent provided the highest yield of 4-bromo-3-phenylisoquinoline (**2a**) (method A), and 2 equiv. of HOAc as additive and a mixture CH_2ClCH_2Cl/H_2O(50:1) as solvent gave the highest yield of 4-bromo-3-phenylisoquinolin-1(2*H*)-one (**3a**) (method B) (entries 1 and 7).

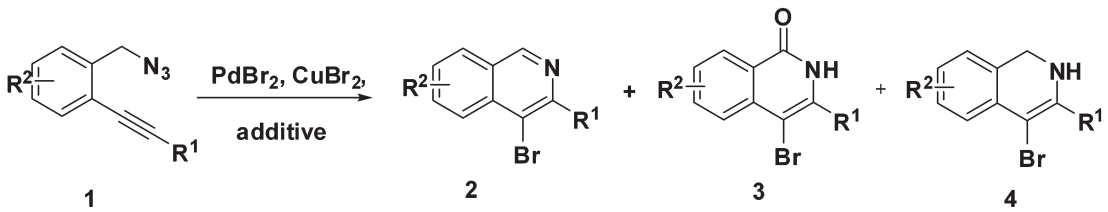
As shown in Table 2, the scope of 2-alkynylbenzyl azides **2** for the halopalladation cyclisation reaction was explored under the standard reaction conditions. In the case of the method

Table 1 Annulation of 2-phenylethynyl benzyl azide (**1a**) in presence of $PdBr_2$[a]



Entry	Additive/equiv.	Solvent	Time/h	Yield/%[b]	
				2a	**3a**
1	LiBr (2)	MeCN	26	65	Trace
2	LiBr (2)	$ClCH_2CH_2Cl$	26	31	18
3	LiBr (1)	$ClCH_2CH_2Cl$	26	20	25
4	LiBr (0.2)	$ClCH_2CH_2Cl$	26	12	27
5	HOAc (1)	$ClCH_2CH_2Cl$	22	Trace	40
6	HOAc (2)	$ClCH_2CH_2Cl$	22	Trace	70
7	HOAc (2)/H_2O (0.1 mL)	$ClCH_2CH_2Cl$	22	Trace	83
8	HOAc (2)/H_2O (0.5 mL)	$ClCH_2CH_2Cl$	22	Trace	68

[a]Reaction conditions: **1a** (0.3 mmol), $PdBr_2$ (5 mol%), $CuBr_2$ (3 equiv.) and additive in the indicated solvent (5 mL) at 80 °C.
[b]Isolated yield.



Scheme 1 Synthesis of bromoisoquinoline and bromoisoquinolone.

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A-based cyclisation, substrates **1b**, **1c** and **1h–j** successfully gave the corresponding bromoisoquinolines. Azides with an electron-donating group (compounds **1b** and **1c**) were subjected to method A, and gave 3-substituted 4-bromoisoquinolines **2b** and **2c** in good yields (entries 1 and 2). The aliphatic alkynyl benzyl azides **1h–j** provided good yields of 3-substituted 4-bromo-1,2-dihydroisoquinoline **4h–j** under the same conditions (entries 7–9). For example, under the reaction condition of 5 mol% of $PdBr_2$, 3 equiv. of $CuBr_2$, and 2 equiv. of LiBr, a 78% yield of 4-bromo-3-(4-methoxyphenyl)isoquinoli ne (**2b**) was obtained, and a 68% yield of 4-bromo-3-octyl-1,2-dihydroisoquinoline (**4h**) was obtained (entries 2 and 7).

In the presence of 5 mol% of $PdBr_2$, 3 equiv. of $CuBr_2$, and 2 equiv. of HOAc, palladium-catalysed annulations of 2-alkynylbenzyl azides (**1b–g**) provided moderate to good yields of the corresponding 3-substituted 4-bromoisoquinolin-1(2*H*)-one (**3b–g**). As shown in Table 2, substituents affected the selectivity of reactions. The results showed that electron-withdrawing groups in the aromatic ring connecting with alkyne favored the desired reaction, but an electron-donating group suppressed it (entries 1–3). For example, the substrate **1d** bearing a nitro group gave 81% yield of the target product **3d** exclusively in the presence of $PdBr_2$ and $CuBr_2$, whereas the substrate **1c** bearing a methoxyl group provided the desired product **3c** in 42% yield (entries 1 and 3). The 2-heteroarylethynylbenzyl azides (**1e**) successfully underwent the cyclisation to afford the dibromo-addition product **3e** in moderate yield (entry 4). Substrates with the aromatic ring bearing a substituted group **1f** and **1g** were compatible with annulations, provided products **3f** and **3g** in 57% and 59% yield, respectively. (entries 5 and 6). However, when the aliphatic alkynyl benzyl azides (**1h–j**) were subjected to method B the expected products were not obtained (entries 7–9).

In summary, an efficient selective synthesis method has been developed for the synthesis of 4-bromoisoquinolines and 4-bromoisoquinolin-1(2*H*)-ones. In the presence of $PdBr_2$, $CuBr_2$, and additive, a variety of 2-alkynyl benzyl azides smoothly underwent the halopalladation cyclisation to afford the corresponding 4-bromoisoquinolines and 4-bromoisoquinolin-1(2*H*)-ones in moderate to good yields. Most importantly, these isoquinolines and isoquinolones with a halo group would be useful introduction of various functional groups, which should be significant for drug discovery.

Experimental

CAUTION: Many low-molecular-weight azides are explosive. In this lab, no problems have been encountered, but great caution should be exercised when heating compounds of this type, especially neat. The reactions described here were run on only a few grams; an increase in the scale of these reactions will decrease the efficiency of heat dissipation and explosions may result.

NMR spectra were obtained with an INOVA-400 (Varian) and AMX-400 (Bruker) spectrometer, operating at 400 MHz (^{1}H NMR) and 100 MHz (^{13}C NMR). TMS was used an internal standard and $CDCl_3$ was used as the solvent. Mass spectrometric analysis was performed on a GC-MS instrument (Shimadzu GCMS-QP2010 plus). Melting points were recorded on an Electrothermal type 9100 melting point apparatus. All melting points are uncorrected.

Synthesis of 3-substituted 4-bromoisoquinolines (**2**) *and 3-substituted 4-bromo-1,2-dihydroisoquinoline* (**4**); *typical procedure*

A mixture of the 2-alkynyl benzyl azide **1** (0.3 mmol), $PdBr_2$ (5 mol %), $CuBr_2$ (3 equiv.), LiBr (2 equiv.) and CH_3CN (5 mL) was stirred at the indicated reaction temperature until consumption of the starting material was complete as judged by TLC and GC analysis. Then the mixture was filtered and evaporated, the residue was purified by flash column chromatography to afford 2 and **4** (hexane/ethyl acetate).

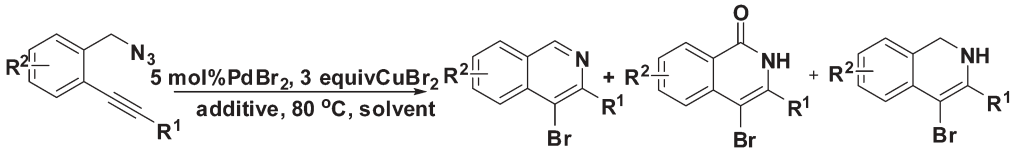
Synthesis of 3-substituted 4-bromoisoquinoline 1(2H)-ones (**3**); *typical experimental procedure*

A mixture of the 2-alkynyl benzyl azides **1** (0.3 mmol), $PdBr_2$ (5 mol %), $CuBr_2$ (3 equiv.), HOAc (2 equiv.), H_2O (0.1 mL) and $ClCH_2CH_2Cl$ (5 mL) was stirred at the indicated reaction temperature until consumption of the starting material was complete as judged by TLC and GC analysis. Then the mixture was filtered and evaporated, the residue was purified by flash column chromatography to afford **3** (hexane/ethyl acetate).

4-Bromo-3-phenylisoquinoline (**2a**):[35,36] Colourless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.23 (s, 1H), 8.33 (d, *J* = 8.5 Hz, 1H), 8.01 (d, *J* = 8.0 Hz, 1H), 7.84 (t, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 8.5 Hz, 2H), 7.68 (t, *J* = 8.0 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 2H), 7.45 (t, *J* = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.3, 151.1, 140.7, 136.0, 131.9, 129.9, 128.6, 128.3, 127.9, 127.7, 127.0, 118.3; LRMS (EI, 70 eV) *m/z* (%): 285 (M^++2, 23), 283 (M^+, 25), 204 (-Br, 100).

4-Bromo-3-o-tolylisoquinoline (**2b**): Orange solid, m.p. 110.2–111.6 °C (uncorrected); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.24 (s, 1H), 8.30 (d, *J* = 8.5 Hz, 1H), 8.03 (d, *J* = 8.5 Hz, 1H), 7.85 (t, *J* = 8.3 Hz, 1H), 7.70 (t, *J* = 8.0 Hz, 1H), 7.38–7.30 (m, 4H), 2.16 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.3, 151.0, 140.7, 135.9, 135.6, 131.8, 130.1, 129.0, 128.6, 128.4, 127.9, 127.8, 126.6, 125.6, 119.5, 19.5; LRMS (EI, 70 eV) *m/z* (%): 299 (M^++2, 8), 297 (M^+, 8), 218 (-Br, 100); HRMS (EI) for $C_{16}H_{12}{}^{79}BrN$ (M^+): calcd 297.0153, found 297.0150.

Table 2 Effect of 2-alkynylbenzyl azides on the reaction selectivity[a]



1 2 3 4

Entry	1[d]	Time/h	Method A		Method B	
			Ratio[b] (2/3)	Yield/%[c,d]	Ratio[b] (2/3)	Yield/%[c,d]
1	R^2 = H, R^1 = *o*-MeC_6H_4 (**1b**)	20	88/12	72 (**2b**)	45/55	38 (**3b**)
2	R^2 = H, R^1 = *p*-$MeOC_6H_4$ (**1c**)	20	90/10	78 (**2c**)	39/61	42 (**3c**)
3	R^2 = H, R^1= *p*-$NO_2C_6H_4$ (**1d**)	34	0/0	Trace	100/0	81 (**3d**)
4	R^2 = H, R^1 = 2-thiophene (**1e**)	22	0/0	Trace	100/0	76 (**3e**)[E]
5	R^2 = 3-MeO, R^1 = C_6H_5 (**1f**)	24	0/0	Trace	100/0	57 (**3f**)
6	R^2 = 3, 4-dimethoxy, R^1 = C_6H_5 (**1g**)	24	0/0	Trace	100/0	59 (**3g**)
7	R^2 = H, R^1 = *n*-C_8H_{17} (**1h**)	22	100/0 (4/3)	68 (**4h**)	0/0	Trace
8	R^2 = H, R^1 = *n*-C_5H_{11} (**1i**)	22	100/0 (4/3)	62 (**4i**)	0/0	Trace
9	R^2 = H, R^1 = 1-cyclohexenyl (**1j**)	24	100/0 (4/3)	60 (**4j**)	0/0	Trace

[a] Reaction conditions of method A: **1** (0.3 mmol), $PdBr_2$ (5 mol%), $CuBr_2$ (3 equiv.) and LiBr (2 equiv.) in MeCN (5 mL) 80 °C. Reaction conditions of method B: **1** (0.3 mmol), $PdBr_2$ (5 mol%) and HOAc (2 equiv.) in $ClCH_2CH_2Cl$ (5 mL) and H_2O (0.1 mL) at 80 °C.
[b] Calculated by using LC/MS. [c] Isolated yield. [d] All of the new compounds were characterised by ^{1}H NMR and ^{13}C NMR spectra as given in the Electronic Supplementary Information. [e] **3e** is 4-bromo-3-(5-bromothiophen-2-yl)isoquinolin-1(2H)-one.

4-Bromo-3-(4-methoxyphenyl)isoquinoline (**2c**): Orange solid, m.p. 109.8–110.9 °C (uncorrected); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.21 (s, 1H), 8.32 (d, *J* = 9.0 Hz, 1H), 7.98 (d, *J* = 3.0 Hz, 1H), 7.82 (t, *J* = 8.3 Hz, 1H), 7.72 (d, *J* = 8.5 Hz, 2H), 7.66 (t, *J* = 8.0 Hz, 1H), 7.03 (d, *J* = 9.5 Hz, 2H), 3.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.7, 152.0, 151.0, 136.1, 133.1, 131.8, 131.4, 128.4, 127.7, 127.6, 126.9, 118.0, 113.4, 55.3; LRMS (EI, 70 eV) *m/z* (%): 315 (M^++2, 45), 313 (M^+, 47), 234 (-Br, 62), 219 (41); HRMS (EI) for $C_{16}H_{12}{}^{79}BrNO$ (M^+): calcd 313.0102, found 313.0100.

4-Bromo-3-phenylisoquinolin-1(2H)-one (**3a**):[37] White solid, m.p. 158.4–158.6 °C (uncorrected); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.83 (d, *J* = 7.5 Hz, 1H), 7.54–7.48 (m, 5H), 7.42 (t, *J* = 7.5 Hz, 1H), 7.27 (t, *J* = 7.5 Hz, 1H), 6.64 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.1, 137.5, 135.2, 133.5, 132.2, 131.1, 130.2,130.1, 129.3, 129.1, 123.9, 122.8, 103.6; LRMS (EI, 70 eV) *m/z* (%): 301 (M^++2, 43.8), 299 (M^+, 49.1), 220 (-Br, 100.0).

4-Bromo-3-o-tolylisoquinolin-1(2H)-one (**3b**): White solid, m.p. 172.4–172.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.44–7.40 (m, 2H), 7.36–7.30 (m, 3H), 7.27–7.24 (m, 2H), 6.27 (d, *J* = 8.0 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 137.8, 136.5, 135.2, 133.9, 132.6, 131.0, 130,4, 130.2, 129.3, 128.5, 126.9, 123.9, 122.4, 102.8; LRMS (EI, 70 eV) *m/z* (%): 315 (M^++2, 13.1), 313 (M^+, 15.8), 234 (-Br, 37.3), 216 (21.5). HRMS (EI) for $C_{16}H_{12}{}^{79}BrNO$ (M^+): calcd 313.0102, found 313.0100.

4-Bromo-3-(4-methoxyphenyl)isoquinolin-1(2H)-one (**3c**): White solid, m.p. 168.5–168.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.45–7.41 (m, 3H), 7.30 (t, *J* = 7.4 Hz, 1H), 6.70 (d, *J* = 8.4 Hz, 2H), 6.74 (d, *J* = 8.0 Hz, 1H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 135.3, 134.3, 133.3, 132.2, 131.7, 131.1, 129.7, 129.2, 123.8, 122.8, 114.6, 104.3, 55.5; LRMS (EI, 70 eV) *m/z* (%): 331 (M^++2, 46.9), 329 (M^+, 40.9), 250 (-Br, 100). HRMS (EI) for $C_{16}H_{12}{}^{79}BrNO_2$ (M^+): calcd 329.0051, found 329.0050.

4-Bromo-3-(4-nitrophenyl)isoquinolin-1(2H)-one (**3d**): Brown solid, m.p. 252.1–252.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.36 (d, *J* = 11.0 Hz, 2H), 7.92 (s, 1H), 7.86 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 10.5 Hz, 2H), 7.51–7.47 (m, 1H), 7.35–7.29 (m, 1H), 6.69 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.8, 144.0, 134.9, 134.5, 132.6, 131.6, 131.1, 130,1, 130.0, 124.4, 124.1, 122.5, 99.4; LRMS (EI, 70 eV) *m/z* (%): 346 (M^++2, 91.0), 344 (M^+, 93.9), 316 (15.9), 236 (12.1), 219 (100). HRMS (EI) for $C_{15}H_9{}^{79}BrN_2O_3$ (M^+): calcd 343.9797, found 343.9795.

4-Bromo-3-(5-bromothiophen-2-yl)isoquinolin-1(2H)-one (**3e**): Brown solid, m.p. 161.5–161.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.5 Hz, 1H), 7.89 (s, 1H), 7.84 (d, *J* = 7.5 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 1H), 7.42 (t, *J* = 8.0 Hz, 1H), 7.09 (d, *J* = 3.5 Hz, 1H), 7.01 (t, *J* = 5.75 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.9, 140.6, 136.6, 134.7, 132.7, 130.9, 130.7, 130.5, 130.3, 130.0, 124.1, 123.0, 116.3; LRMS (EI, 70 eV) *m/z* (%): 387 (M^++4, 8.2), 385 (M^++2, 15.5), 383 (M^+, 10.2), 306 (-Br, 11.6), 304 (-Br, 11.3), 225 (-2Br, 41.3). HRMS (EI) for $C_{13}H_7{}^{79}Br_2NOS$ (M^+): calcd 382.8615, found 382.8613.

4-Bromo-7-methoxy-3-phenylisoquinolin-1(2H)-one (**3f**): White solid, m.p. 168.4–168.8 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.58–7.51 (m, 5H), 7.33 (t, *J* = 2.0 Hz, 1H), 6.86 (d, *J* = 10.0 Hz, 1H), 6.70 (d, *J* = 9.0 Hz, 1H), 3.86 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.9, 160.8, 136.0, 132.4, 131.3, 130.2, 129.9, 129.1, 127.9, 123.9, 120.4, 111.7, 106.4, 55.7; LRMS (EI, 70 eV) *m/z* (%): 331 (M^++2, 11.8), 329 (M^+, 11.1), 250 (-Br, 8.7). HRMS (EI) for $C_{16}H_{12}{}^{79}BrNO_2$ (M^+): calcd 329.0051, found 329.0050.

4-Bromo-6,7-dimethoxy-3-phenylisoquinolin-1(2H)-one (**3g**): White solid, m.p. 171.4–171.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.55–7.45 (m, 5H), 7.23 (s, 1H), 6.01 (s, 1H), 3.91 (s, 3H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 152.5, 150.7, 137.7, 133.7, 130.4, 129.7, 129.2, 129.1, 124.0,104.9, 101.7, 77.3, 56.3, 55.6; LRMS (EI, 70eV) *m/z* (%): 361 (M^++2, 14.8), 359 (M^+, 13.1), 280 (-Br, 9.9). HRMS (EI) for $C_{17}H_{14}{}^{79}BrNO_3$ (M^+): calcd 359.0157, found 359.0153.

4-Bromo-3-octyl-1,2-dihydroisoquinoline (**4h**): Colourless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (t, *J* = 8.75 Hz, 1H), 7.38–7.35 (m, 2H), 7.22 (t, *J* = 4.5 Hz, 1H), 4.42–4.34 (m, 2H), 2.90–2.82 (m, 2H), 1.72–1.68 (m, 2H), 1.45–1.31 (m, 10H), 0.90 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.1, 133.0, 129.4, 129.3, 128.7, 128.6, 126.5, 113.6, 52.0, 40.3, 31.8, 29.3, 29.2, 28.6, 27.5, 22.6, 14.1; LRMS (EI, 70 eV) *m/z* (%): 321 (M^++2, 2), 319 (M^+, 2), 237 (2), 236 (11), 235 (3), 223 (97), 220 (100); HRMS (EI) for $C_{17}H_{24}{}^{79}BrN$ (M^+): calcd 321.1092, found 321.1089.

4-Bromo-3-pentyl-1,2-dihydroisoquinoline (**4i**): Colourless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43–7.34 (m, 3H), 7.22 (t, *J* = 4.5 Hz, 1H), 4.43–4.34 (m, 2H), 2.91–2.79 (m, 2H), 1.75–1.69 (m, 2H), 1.45–1.39 (m, 4H), 0.96 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.1, 133.0, 129.4, 129.3, 128.8, 128.6, 126.5, 113.6, 52.0, 40.3, 30.7, 27.2, 22.4, 14.0; LRMS (EI, 70 eV) *m/z* (%): 281 (M^++2, 2), 279 (M^+, 2), 223 (57), 221 (59), 199 (16), 198 (100), 197 (15); HRMS (EI) for $C_{14}H_{18}BrN$ (M^+): calcd 279.0623, found 279.0625.

4-Bromo-3-cyclohexenyl-1,2-dihydroisoquinoline (**4j**): Pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44–7.36 (m, 3H), 7.28–7.26 (m, 1H), 6.06 (t, *J* = 7.5 Hz, 1H), 4.48–4.39 (m, 2H), 2.29–2.26 (m, 2H), 2.20–2.16 (m, 2H), 1.79–1.74 (m, 2H), 1.68–1.65 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.8, 137.1, 133.0, 131.8, 131.2, 129.3, 128.8, 1127.9, 124.6, 112.6, 52.0, 26.4, 25.2, 22.3, 21.6; LRMS (EI, 70 eV) *m/z* (%): 291 (M^++2, 26), 289 (M^+, 26), 260 (-Br, 11), 259 (29), 258 (10); HRMS (EI) for $C_{15}H_{16}{}^{79}BrN$ (M^+): calcd 289.0466, found 289.0462.

Electronic Supplementary Information

^{1}H NMR and ^{13}C NMR spectra of the new compounds have been deposited in the ESI available through stl.publisher.ingentaconnect.com/content/stl/jcr/supp-data.

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