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Microwave assisted Leimgruber–Batcho reaction for the preparation of indoles, azaindoles and pyrroylquinolines

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The development of enhanced conditions for Lewis acid catalysed Leimgruber–Batcho indole synthesis using microwave acceleration is described. This approach has permitted the preparation of a variety of heteroaromatic enamine intermediates in good yield and high purities. Subsequent catalytic hydrogenation reactions, under various conditions including the use of a solid-phase encapsulated catalyst, furnish the corresponding indole derivatives in good yields.

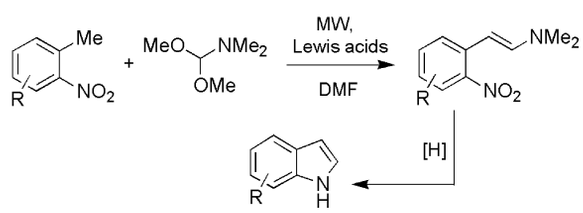
Introduction

Microwave-assisted chemical synthesis is proving to be a powerful technique for increasing the throughput of chemical reactions.[1,2] Specific approaches such as focused microwave flash heating, involving elevated temperatures and pressures attained in sealed reactors, has proven especially useful for achieving faster reactions and the formation of cleaner products.[3,4] We have applied this form of microwave dielectric heating as the primary means of accelerating a diverse range of reactions in order to maximise the quantities of material that can be progressed through a synthetic sequence. This has been of particularly value in reactions mediated by solid-supported reagents, examples include a polymer-supported thionating agent,[5] a supported reagent for the conversion of isothiocyanates to isocyanides[6] and in the formation of natural products such as (±)-epibatidine,[7] (+)-plicamine[8] and (+)-didemniserinolipid B.[9] Due to the power and synthetic expedience of this microwave methodology, we have expanded our investigations to include other traditional reactions which are known to be problematic due to the necessity for harsh reaction conditions.

The biological importance of indoles and related motifs in both natural products[10] and many pharmaceutical compounds[11] means these systems are of special interest to synthetic chemists. Indeed pyrroloquinolines have recently been found to be especially useful in a variety of medicinal applications.[12] However, there are few synthetic approaches to these polycyclic aromatic structures in the literature.[13] One powerful procedure is the Leimgruber–Batcho synthesis of indoles,[14] although the reaction suffers from the requirement of prolonged reaction times and high reaction temperatures. Here, we wish to describe the successful modification of this reaction to the formation of indole, azaindole and pyrroloquinoline derivatives using microwave-assisted organic synthesis to accelerate compound production.

Results and discussion

The Leimgruber–Batcho synthesis is a widely used method for the preparation of indole containing structures.[11b,15] The reaction depends on the acidity of a methyl group positioned adjacent to an aromatic nitro group (or critically at the α or γ positions on a pyridine ring). A direct condensation reaction with dimethylformamide (DMF) or more commonly dimethylformamide dimethyl acetal (DMFDMA) under acid catalysis facilitates the introduction of the future indole α-carbon as the enamine. Subsequent catalytic reduction of the nitro group leads to spontaneous cyclisation and formation of the corresponding indole derivative (Scheme 1). Under conventional conditions the first condensation reaction usually requires overnight heating in DMF which often leads to less than optimal yields due to product instability and solvent degradation.



Scheme 1 The Leimgruber–Batcho synthesis of indoles.

We began our study by examining the direct condensation of nitrotoluene and DMFDMA (Scheme 1; R = H) as the standard reaction thus avoiding any possible complications due to additional electronic or dipolar effects.[4c] The literature reported reaction using conventional thermal heating (110 °C for 22 h) yielded the enamine adduct in 97% yield.[14b] In contrast, using microwave heating conditions (180 °C for only 4.5 h) we obtained the same product in quantitative conversion and 95% isolated yield following a rapid purification by filtration through a plug of silica gel. At this stage no further optimisation was carried out on either the reaction conditions (time/temperature/pressure) or isolation method.

Although the microwave induced reaction demonstrated a marked improvement in terms of the overall reaction time, an additional study was conducted to investigate the possible effects of Lewis acid catalysis on the further enhancement of the microwave reaction. A variety of transition metal catalysts were screened as described in Table 1. It was found that both anhydrous CuI and $Yb(OTf)_3$ were effective catalysts giving the best overall yields and highest purities within the shortest reaction times. In the subsequent reactions CuI was adopted as the catalyst of choice due to its higher conversion and lower cost (Table 1). In order to standardise the reaction conditions, the volume in the Emrys Liberator™ microwave tube[16] was kept constant for all the examples. The recorded pressure attained during the course of the irradiation was within the range of 8–10 bar.

It is interesting to note that the addition of a small quantity of DMF greatly enhanced the reaction rate, possibly due to better microwave absorption as indicated by a more steeply rising temperature profile. Decomposition of DMF has also been noted at such high reaction temperatures in the presence

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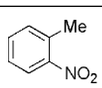
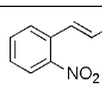
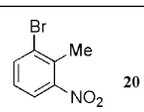
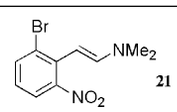
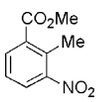
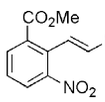
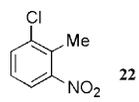
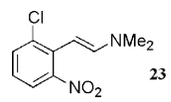
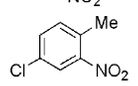
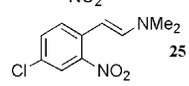
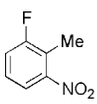
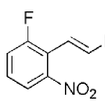
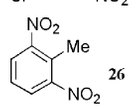
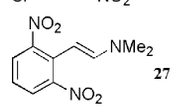
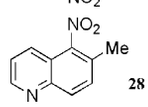
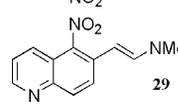
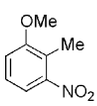
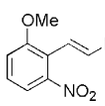
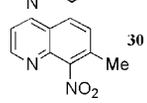
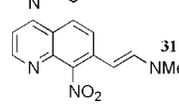
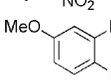
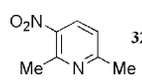
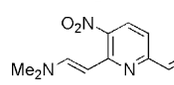
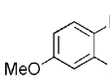
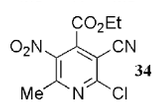
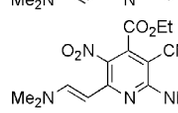
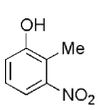
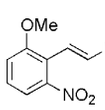
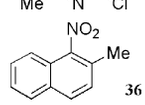
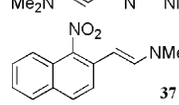
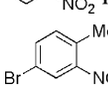
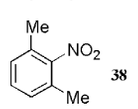
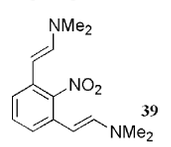
Table 1 Screening of Lewis acids and additives for Leimgruber–Batcho reaction by ^{1}H NMR

Time (min)	Reaction temp.	Catalysts and additives	Conversion yields
270	180 °C	Without pulsing, no catalyst	100%
30 × 7	180 °C	No catalyst	100%
20 × 6	185 °C	CuI (0.02 eq.)	98%
165	180 °C	Without pulsing, CuI (0.02 eq.)	99%
30 × 7	185 °C	DABCO (0.3 eq.)	93%
30 × 2	185 °C	CuI (0.04 eq.), DMAP (cat.)	85%
10 × 4	180 °C	Cu(I)OTf·C_6H_6 (0.04 eq.), DMAP (cat.)	86%
20 × 3	175 °C	$Yb(OTf)_3$ (0.05 eq.), DABCO (cat.)	88%
20 × 3	175 °C	$Zn(OTf)_2$ (0.05 eq.), DABCO (0.04 eq.)	90%
20 × 10	170 °C	CuI (0.03 eq.), Cs_2CO_3 (0.04 eq.)	90%
30 × 6	185 °C	CuBr (0.02 eq.)	93%

Table 2 Microwave-assisted Leimgruber–Batcho enamine formation

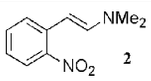
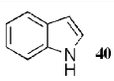
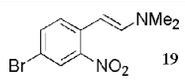
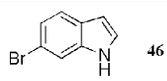
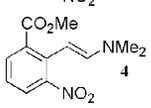
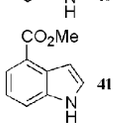
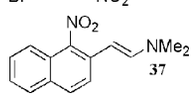
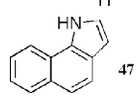
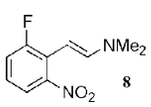
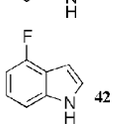
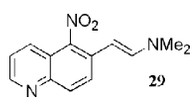
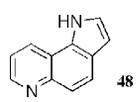
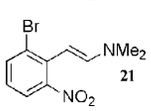
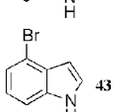
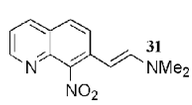
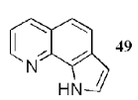
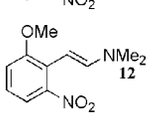
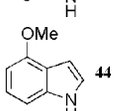
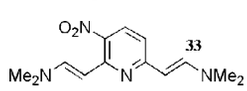
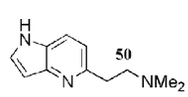
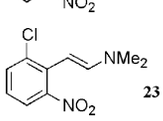
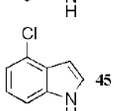
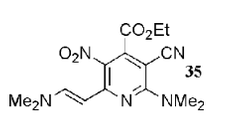
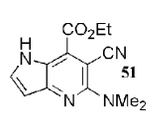
Entry	Substrate	Product	Yield (%)	Time (min)	Entry	Substrate	Product	Yield (%)	Time (min)
1	 **1**	 **2**	98%	20 × 6	11	 **20**	 **21**	Not isolated	20
2	 **3**	 **4**	92%	20 × 2	12	 **22**	 **23**	89%	20
3	 **5**	 **6**	90%	10	13	 **24**	 **25**	90%	10
4	 **7**	 **8**	85%	20	14	 **26**	 **27**	85%	10
5	 **9**	 **10**	82%	20	15	 **28**	 **29**	90%	17
6	 **11**	 **12**	83%	20 × 9	16	 **30**	 **31**	92%	20
7	 **13**	 **14**	70%	20	17	 **32**	 **33**	95%	20
8	 **15**	 **16**	74%	20 × 9	18[a]	 **34**	 **35**	Not isolated	17
9	 **17**	 **12**	54%	600 (10 h)	19	 **36**	 **37**	85%	20 × 2
10	 **18**	 **19**	Not isolated	20	20	 **38**	 **39**	—	—

[a] The homologation of this compound requires the use of DMF diethyl acetal, so as to prevent any transesterification.

of metal catalysts, leading to the formation of carbon monoxide and dimethylamine.[17] The generation of these volatile components is undoubtedly responsible for the rapidly increasing pressure profile during the course of the reactions. As a consequence the reaction kinetics would be expected to be enhanced especially for the case of a condensation reaction.

Table 2 lists the enamines formed as intermediates from the Leimgruber–Batcho reaction. Microwave irradiation of nitrotoluene with DMFDMA in the presence of anhydrous CuI at 180 °C gave the corresponding enamine in 98% yield as a dark red oil (Table 2; Entry 1). Workup of the reaction involved only a simple filtration and elution with CH_2Cl_2 through a bond elut silica cartridge,[18] followed by solvent removal under high vacuum. As we have previously noted in other chemistries,[19] the application of short bursts of microwave heating can be more effective than a single prolonged heating profile (Table 1). However, this effect was in this chemistry less significant than individual substrate differences resulting from the substituents on the aromatic systems. Those bearing an electron-rich methoxy group where less reactive and required longer reaction times. Conversely, aromatic systems with strongly electron withdrawing groups such as a nitrile **5** (Table 2; Entry 3) or a second nitro unit **26** (Table 2; Entry 14) gave the corresponding enamines in high yield after only 10 min. Similarly, quinolines and other pyridyl-related structures which are electron deficient in nature showed dramatically increased reaction rates when compared to

Table 3 Reductive cyclisation of enamines to the corresponding indole derivatives (by Pd/C in MeOH)

Entry	Substrate	Product	Yield (%)	Entry	Substrate	Product	Yield (%)
1	 **2**	 **40**	75%	7	 **19**	 **46**	52%[a]
2	 **4**	 **41**	65%	8	 **37**	 **47**	90%
3	 **8**	 **42**	60%	9	 **29**	 **48**	75%[b]
4	 **21**	 **43**	67%[a]	10	 **31**	 **49**	80%[b]
5	 **12**	 **44**	63%	11	 **33**	 **50**	70%[b]
6	 **23**	 **45**	74%[a]	12	 **35**	 **51**	63%[b,c]

[a] Reduction was done by refluxing Zn/AcOH. [b] Reduction was done by 10–15 mol% of the Pd/C catalyst in the presence of a small amount of acetic acid. [c] An X-ray crystal structure was obtained for compound **51**.[20]

those of the simple phenyl systems (*cf.* Table 2; Entries 1, 2 and 15–18). All the enamine intermediates were confirmed as the *trans* configured geometry as determined by ^{1}H NMR spectroscopy. Furthermore, X-ray diffraction studies of single crystals of **6**, **29**, **31**, **33** (Table 2; Entries 3, 15, 16 and 17), were also used to confirm the exclusive *trans*-configuration.[20]

Not all the substrates tested proved as susceptible to manipulation, we encountered several difficulties in the preparation of enamine **35** (Table 2; Entry 18). The reactive α-chloro functionality of pyridine **34** was readily substituted by a dimethylamino unit, which is perceived to arise from the decomposition of the DMF or the DMF acetal. It was also found necessary to use the alternative dimethylformamide diethyl acetal (DMFDEA) for the homologation of this compound in order to prevent additional transesterification of the pendant methyl ester functionality. Finally, enamine **35** was also found to be unstable when isolation was attempted and it was therefore subjected to the cyclisation conditions to generate the indole without prior purification.

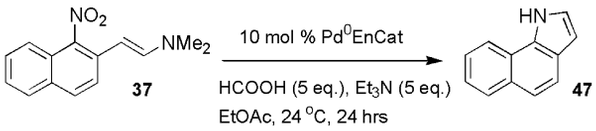
Both the 4- and 6-bromonitrotoluenes (Table 2; Entries 10 and 11) reacted rapidly with DMFDMA to give a dark red oil, however after the usual workup they did not give pure products as indicated by ^{1}H NMR. Instead the products were accompanied by substantial quantities of polyaromatics.[21] We initially envisaged that this was a result of unwanted copper catalysed polymerisation reactions. Therefore, in an attempt to circumvent this problem we substituted the usual copper catalyst for $Yb(OTf)_3$. This did significantly improve the reaction mixture composition but did not fully alleviate the problem. Carrying the unpurified material through to the next stage proved to be the only viable option and following reductive cyclisation gave an acceptable yield of the indole product. Interestingly, the chloro derivatives **22** and **23** (Table 2; Entries 12 and 13) showed the same rapid reactions but without the propensity for generating the same complex mixtures.

Entry 9 (Table 2) also deserves a mention. Hydroxynitrotoluene **17** reacted initially with the DMFDMA to undergo methylation of the phenol, a reaction that has been reported previously in the literature.[22] Subsequent conversion to the corresponding enamine **12** (Table 2; Entry 9) was extremely slow, yielding only 54% of the desired product even after 10 h of irradiation. Further heating or modification of the heating parameters failed to improve the yield, resulting in the formation of higher levels of by-products. In contrast to the literature [14a,22a,b] we were able to successfully isolate this material for full characterisation.

A selection of the isolated enamine intermediates were subjected to catalytic hydrogenation using 10% Pd/C in MeOH (Table 3). Filtration of the catalyst, and removal of the solvent *in vacuo* gave the corresponding indoles in good yields. However, halogen containing enamines (Table 3; Entries 4, 6 and 7) required refluxing Zn/AcOH for reductive cyclisation to occur.[2a,b] These methods were also extended to the preparation of azaindoles and pyrroloquinolines. It was interesting to note that for entry 17 (Table 2), where a double homologation was observed on nitropyridine **32**, the corresponding enamine underwent reductive cyclisation with concomitant reduction of the electron rich double bond at the 5 position of the pyridyl ring to furnish the corresponding azaindole **50** (Table 3). For entry 18 (Table 2), the crude enamine was used without purification, therefore column chromatography was required after the reductive cyclisation to obtain the pure product **51** in 60% yield. For cyclisation to the azaindoles and pyrrolquinolines, a small amount of acetic acid was added to prevent any catalyst poisoning by the substrates.

Recently we reported the development of a system for the reduction of aromatic nitro groups by transfer hydrogenation, using an encapsulated nanoparticulate Pd catalyst, HCOOH and Et_3N as the reducing agents.[24,25] We have successfully transferred this protocol to the reductive cyclisation of various enamine derivatives. For example, *trans*-2-[β-(dimethylamino)-vinyl]-nitronaphthalene **37** was smoothly converted to the corresponding 1*H*-benz[*g*]indole **47** in 78% yield (Scheme 2). Hydrogenation of the aromatic nitro group was carried out with 6 mol% of Pd-EnCat™, using 5 eq. of a mixture of HCOOH/Et_3N. The immobilised catalyst could easily be recycled without any noticeable loss of catalytic activity. In addition, this reaction can be accelerated to completion within 2 h by microwave irradiation at 120 °C. The combined use of microwave accelerated enamine formation and the use of a recyclable

catalyst for reductive cyclisation in the Leimgruber–Batcho reaction provides a clean synthesis of indoles that would find particular use in an industrial setting.



Scheme 2 Reductive cyclisation using Pd-EnCat™.

Conclusion

An efficient synthesis of indoles, azaindoles and pyrroloquinolines using a Leimgruber–Batcho process where the reaction is conducted by focused microwave heating is reported. The presence of Lewis acids greatly reduce the reaction times and give much better quality of products when compared with conventional heating methods.

Experimental

General

Melting points were determined on a Reichert hot stage apparatus and are reported uncorrected. ^{1}H and ^{13}C NMR spectra were recorded either on a Brüker DRX-600 or on a DPX-400 instrument with $CHCl_3$ (δ = 7.26) and $CDCl_3$ (δ = 77.0) as internal reference signals. Signals were assigned by means of DEPT and 2D spectra (COSY, HMQC, HMBC). IR spectra were recorded on a Perkin-Elmer 'Spectrum-One' spectrometer equipped with an Attenuated Total Reflectance (ATR) sampling accessory. Mass spectra were recorded on a Kratos – TOF spectrometer or a Bruker BIOAPEX 4.7 FTICR spectrometer using electrospray (ESI) or electron impact (EI) techniques (the matrix was *m*-nitrobenzyl alcohol (NOBA)) at the Department of Chemistry, University of Cambridge: relative abundances and assignments are given in parentheses. LC-MS was performed on a Hewlett Packard HPLC 1100 chromatograph (Mercury hexylphenyl column) attached to a HP LC/MSD platform LC APCI mass spectrometer. Reactions were monitored using TLC on precoated glass-backed plates (Merck Kieselgel 60 F254) and visualised by UV. Microanalyses were determined in the microanalytcal laboratories at the Department of Chemistry, University of Cambridge.

General procedure for the synthesis of enamine derivatives

A solution of the 2-nitrotoluene derivative (3.65 mmol) and copper(I) iodide (2 mol%) in a mixture of DMFDMA (5 mL; 37.6 mmol) and DMF (0.1 mL) was heated at 180 °C in a sealed vial under microwave irradiation (20 min × 7);[16] an internal pressure of 8–10 bar was observed during the heating sequence. The crude reaction mixture was directly filtered through a pre-packed silica bond elut cartridge[18] (22 mm in diameter, 2 g silica), and eluted with either CH_2Cl_2 (10 mL × 3) or EtOAc (10 mL × 3) for the more polar systems. The combined filtrates were concentrated under reduced pressure to yield the corresponding enamine products without the need for further purification.

trans-2-[β-(Dimethylamino)vinyl]-nitrobenzene (2)[26]

Dark red oil, 98% yield, R_f = 0.56 (light petroleum : Et_2O = 1 : 1); δ_H(400 MHz; $CDCl_3$) 7.81 (1H, d, *J* 8 Hz, H-6), 7.42 (1H, d, *J* 9 Hz, H-3), 7.30 (1H, t, *J* 8 Hz, H-4), 6.95 (1H, t, *J* 8 Hz, H-5), 6.87 (1H, d, *J* 14 Hz, ArCHC*H*NMe_2), 5.83 (1H, d, *J* 14 Hz, ArC*H*CHNMe_2), 2.94 (6H, s, NMe_2); δ_C(100 MHz; $CDCl_3$) 145.22 (C-1), 144.57 (ArCH*C*HNMe_2), 135.74 (C-2), 132.39 (C-4), 125.34 (C-6), 124.39 (C-3), 122.44 (C-5), 91.30 (Ar*C*H-CHNMe_2), 40.67 (NMe_2); ν_{max}(neat)/cm^{-1} 3400, 1620, 1594, 1505, 1094, 941, 777, 738; *m*/*z* (EI) 192.08929 (M^+, $C_{10}H_{12}N_2O_2$ requires 192.08988); 192.1 (25%) (M^+), 119 (45), 68.9 (100).

Methyl *trans*-2-[β-(dimethylamino)vinyl]-3-nitrobenzoate (4)[14a]

Dark red oil, 92% yield, R_f = 0.43 (light petroleum : Et_2O = 1 : 1); δ_H(400 MHz; $CDCl_3$) 7.75 (2H, m, H-4 and H-6), 7.05 (1H, t,*J* 8 Hz, H-5), 6.35 (1H, d, *J* 14 Hz, ArCHC*H*NMe_2), 6.72 (1H, d, *J* 14 Hz, ArC*H*CHNMe_2), 3.80 (3H, s, OMe), 2.80 (6H, s, NMe_2); δ_C(100 MHz; $CDCl_3$) 168.9 (C=O), 149.1 (C-3), 145.8 (ArCH*C*HNMe_2), 134.0 (C-2), 132.9 (C-6), 131.3 (C-1), 126.54 (C-4), 122.7 (C-5), 88.8 (Ar*C*HCHNMe_2), 52.2 (OMe), 40.4 (NMe_2); ν_{max}(neat)/cm^{-1} 2948, 1719, 1626, 1592, 1520, 1433, 1374, 1256, 1191, 1116, 1092, 954, 767, 739, 704; *m*/*z* (EI) 250.09679 (M^+, $C_{12}H_{14}N_2O_4$ requires 250.09564); 250.1 (25%), (M^+), 181 (100%).

trans-4-[β-(Dimethylamino)vinyl]-3-nitrobenzonitrile (6)[27]

Deep red crystals, 90% yield, R_f = 0.27 (light petroleum : CH_2Cl_2 = 1 : 1); mp 134 °C (lit. mp 134–137.5 °C);[27] (Found: C, 60.06; H, 5.42; N, 17.41 $C_{13}H_{13}N_3O_2$ requires C, 60.21; H, 5.32; N, 17.54%); δ_H(400 MHz; $CDCl_3$) 8.11 (1H, s, H-2), 7.47 (1H, d, *J* 8 Hz, H-6), 7.41 (1H, d, *J* 8 Hz, H-5), 7.20 (1H, d, *J* 14 Hz, ArCHC*H*NMe_2), 5.92 (1H, d, *J* 14 Hz, ArC*H*CHNMe_2), 3.05 (6H, s, NMe_2); δ_C(100 MHz; $CDCl_3$) 147.7 (ArCH*C*HNMe_2), 143.3 (C-3), 140.4 (C-4), 134.0 (C-5), 130.3 (C-2), 123.9 (C-6), 118.1 (C≡N), 103.6 (C-1), 90.0 (Ar*C*HCHNMe_2), 40.1 (NMe_2); ν_{max}(neat)/cm^{-1} 2910, 2214, 1590, 1535, 1434, 1396, 1337, 1260, 1221, 1180, 1102, 1067, 919, 834; *m*/*z* (+ESI) 240.0749 (M + Na, $C_{11}H_{11}N_3O_2$Na requires 240.0749); 241.2 (100%) (M + Na), 224.1 (40%), 200.1 (62%).

3-Fluoro-*trans*-2-[β-(dimethylamino)vinyl]-nitrobenzene (8)[28]

Dark red oil, 85% yield, R_f = 0.54 (light petroleum : CH_2Cl_2 = 1 : 1); δ_H(400 MHz; $CDCl_3$) 7.52 (1H, d, *J* 8 Hz, H-6), 7.26 (1H, d, *J* 14 Hz, ArCHC*H*NMe_2), 7.12 (1H, m, H-4), 6.85 (1H, m, H-5), 5.38 (1H, d, *J* 14 Hz, ArC*H*CHNMe_2), 2.80 (6H, s, NMe_2); δ_C(100 MHz; $CDCl_3$) 158.2 (J_{C-F} 185 Hz, C-3), 147.6 (J_{C-F} 19 Hz, ArCH*C*HNMe_2), 147.1 (J_{C-F} 8 Hz, C-1), 124.2 (J_{C-F} 16 Hz, C-2), 121.0 (J_{C-F}8 Hz, C-5), 120.8 (J_{C-F} 3.3 Hz, C-6), 118.8 (J_{C-F} 25 Hz, C-4), 84.2 (Ar*C*HCHNMe_2), 40.4 (NMe_2); ν_{max}(neat)/cm^{-1} 2906, 2808, 1620, 1570, 1515, 1474, 1380, 1334, 1270, 1211, 1182, 1093, 937, 871, 821 and 799; *m*/*z* (EI) 210.07958 (M^+, $C_{10}H_{11}N_2O_2F$ requires 210.08046), 210.1 (20%) (M^+), 169 (35%); 131 (56%), 86 (65%).

5-Fluoro-*trans*-2-[β-(dimethylamino)vinyl]-nitrobenzene (10)[29]

Dark red oil, 82% yield, R_f = 0.38 (light petroleum : Et_2O = 3 : 2); δ_H(400 MHz; $CDCl_3$) 7.58 (1H, dd, *J* 2.7 Hz, 8 Hz, H-3), 7.95 (1H, dd, *J*6 Hz, 9 Hz, H-6), 7.08 (1H, m, H-4), 6.75 (1H, d, *J* 14 Hz, ArCHC*H*NMe_2), 5.83 (1H, d, *J* 14 Hz, ArC*H*CH-NMe_2), 2.94 (6H, s, NMe_2); δ_C(100 MHz; $CDCl_3$) 156.6 (J_{C-F} 245 Hz, C-5), 144.6 (ArCH*C*HNMe), 132.5 (J_{C-F} 3 Hz, C-2), 126.1 (J_{C-F}7 Hz, C-3), 120.5 (J_{C-F} 23 Hz, C-6), 111.8 (J_{C-F} 23 Hz, C-4), 90.9 (Ar*C*HCHNMe), 40.7 (NMe_2); ν_{max}(neat)/cm^{-1} 2906, 1620, 1515, 1380, 1270, 1211, 1093, 937, 799; *m*/*z* (EI) 210.07947 (M^+, $C_{10}H_{11}N_2O_2F$ requires 210.08046), 210.1 (20%) (M^+), 169 (40%); 131 (50%), 86 (40%).

3-Methoxy-*trans*-2-[β-(dimethylamino)vinyl]-nitrobenzene (12)[14a]

Dark red oil, 83% yield; R_f = 0.52 (light petroleum : Et_2O = 1 : 1); δ_H(400 MHz; $CDCl_3$) 7.40 (1H, d, *J* 14 Hz, ArCHC*H*-NMe_2), 7.22 (1H, m, H-5), 6.93 (2H, m, H-4, H-6), 5.30 (1H, d, *J* 14 Hz, ArC*H*CHNMe_2), 3.80 (3H, s, OMe), 2.80 (6H, s, NMe_2); δ_C(100 MHz; $CDCl_3$) 156.9 (C-3), 148.6 (C-1), 147.2 (ArCH*C*HNMe_2), 124.0 (C-2), 122.4 (C-5), 117.1 (C-6), 113.6 (C-4), 86.6 (Ar*C*HCHNMe_2), 56.4 (OMe), 40.8 (NMe_2);

ν_{max}(neat)/cm^{-1} 2938, 1620, 1586, 1516, 1463, 1365, 1274, 1260, 1227, 1087, 1050, 949, 916, 764, 749; *m/z* (+ESI) 245.0902 (M + Na, $C_{11}H_{14}N_2O_3Na$ requires 245.0902).

4-Methoxy-*trans*-2-[β-(dimethylamino)vinyl]-nitrobenzene (14) [30]

Dark red oil, 70% yield, R_f = 0.48 (light petroleum : EtOAc = 9 : 1); δ_H(400 MHz; $CDCl_3$) 7.91 (1H, *J* 9 Hz, H-6), 6.93 (1H, d, *J* 14 Hz, ArCHC*H*NMe_2), 6.79 (1H, d, *J*2 Hz, H-3), 6.47 (1H, dd, *J* 9 Hz, 2 Hz, H-5), 6.03 (1H, d, *J* 14 Hz, ArC*H*CHNMe_2), 3.83 (3H, s, OMe), 2.89 (6H, s, NMe_2); δ_C(100 MHz; $CDCl_3$) 162.7 (C-4), 145.0 (ArCH*C*HNMe_2), 139.0 (C-2), 138.5 (C-1), 128.3 (C-6), 109.2 (C-5), 107.5 (C-3), 92.3 (Ar*C*HCHNMe_2), 55.6 (OMe), 40.7 (NMe_2); ν_{max}(neat)/cm^{-1} 2903, 1593, 1492, 1235, 1095, 838, 786, 732; *m/z* (+ESI) 245.0902 (M + Na, $C_{11}H_{14}N_2O_3Na$ requires 245.0902); 246 (100%), 234.1 (60%), 205.1 (88%).

5-Methoxy-*trans*-2-[β-(dimethylamino)vinyl]-nitrobenzene (16)

Dark red oil, 74% yield, R_f = 0.44 (light petroleum : CH_2Cl_2 = 1 : 1); δ_H(400 MHz; $CDCl_3$) 7.39 (1H, d, *J* 3 Hz, H-6), 7.35 (1H, d, *J* 9 Hz, H-3), 6.98 (1H, dd, *J* 8 Hz, 2 Hz, H-4), 6.77 (1H, d, *J* 14 Hz, ArCHC*H*NMe_2), 5.84 (1H, d, *J* 14 Hz, ArC*H*CHNMe_2), 3.80 (3H, s, OMe), 2.95 (6H, s, NMe_2); δ_C(100 MHz; $CDCl_3$) 155.3 (C-5), 148.7 (C-1), 143.6 (ArCH*C*HNMe_2), 126.1 (C-3), 123.7 (C-2), 121.4 (C-4), 108.2 (C-6), 91.8 (Ar*C*HCHNMe_2), 56.0 (OMe), 40.7 (NMe_2); ν_{max}(neat)/cm^{-1} 2933, 1622, 1513, 1367, 1286, 1091, 1034, 794; *m/z* (+ESI) 223.1082 (M + H, $C_{11}H_{15}N_2O_3$ requires 223.1083); 223.10 (30%) (M + H), 205.09 (45%), 193.14 (100%).

3-Chloro-*trans*-2-[β-(dimethylamino)vinyl]-nitrobenzene (23) [31]

Dark red oil, 89% yield, R_f = 0.44 (light petroleum : CH_2Cl_2 = 1 : 1); δ_H(400 MHz; $CDCl_3$) 7.45 (1H, d, *J* 8 Hz, H-6), 7.41 (1H, d, *J* 8 Hz, H-4), 6.96 (1H, t, *J* 8 Hz, H-5), 6.68 (1H, d, *J* 14 Hz, ArCHC*H*NMe_2), 5.08 (1H, d, *J* 14 Hz, ArC*H*CHNMe_2), 2.84 (6H, s, NMe_2); δ_C(100 MHz; $CDCl_3$) 148.1 (C-1), 145.8 (ArCH*C*HNMe_2), 133.1 (C-3), 132.7 (C-6), 131.9 (C-2), 123.2 (C-5), 122.3 (C-4), 86.8 (Ar*C*HCHNMe_2), 40.3 (NMe_2); ν_{max}(neat)/cm^{-1} 2894, 1629, 1520, 1373, 1263, 1098, 772, 751, 723; *m/z* (+ESI) 227.05980 (M + H, $C_{10}H_{12}N_2O_2Cl$ requires 227.05873), 227.1 (82%) (M + H), 250.1 (20%).

5-Chloro-*trans*-2-[β-(dimethylamino)vinyl]-nitrobenzene (25) [32]

Dark red oil, 90% yield, R_f = 0.33 (light petroleum : Et_2O = 1 : 1); δ_H(400 MHz; $CDCl_3$) 7.82 (1H, s, H-6), 7.35 (1H, m, H-3), 7.24 (1H, m, H-4), 6.91 (1H, d, *J* 14 Hz, ArC*H*CHNMe_2), 5.79 (1H, d, *J* 14 Hz, ArCHC*H*NMe_2), 2.90 (6H, s, NMe_2); δ_C(100 MHz; $CDCl_3$) 145.2 (ArCH*C*HNMe_2), 144.6 (C-2), 134.7 (C-4), 132.6 (C-6), 127.0 (C-1), 125.4 (C-5), 125.1 (C-3), 90.3 (Ar*C*HCHNMe_2), 40.7 (NMe_2); ν_{max}(neat)/cm^{-1} 2927, 1618, 1597, 1384, 1354, 1256, 1218, 1097, 1030, 893, 879, 821, 760, 737; *m/z* (EI) 226.05163 (M^+, $C_{10}H_{11}N_2O_2Cl$ requires 226.05091); 226.1 (25%) (M^+), 205.1 (20%), 119.0 (45%).

3-Nitro-*trans*-2-[β-(dimethylamino)vinyl]-nitrobenzene (27) [22a]

Deep red crystals, 85% yield, R_f = 0.72 (light petroleum : Et_2O = 7 : 3); mp 94 °C (lit. mp 90–93 °C);[22a] (Found: C, 50.45, H, 4.94, N, 17.47 $C_{10}H_{11}N_3O_4$ requires C, 50.63, H, 4.67, N, 17.71%); δ_H(400 MHz; $CDCl_3$) 8.10 (2H, d, *J* 8 Hz, H-4, H-6), 7.10 (1H, t, *J* 8 Hz, H-5), 6.45 (1H, d, *J* 14 Hz, ArC*H*CHNMe_2), 5.45 (1H, d, *J* 14 Hz, ArCHC*H*NMe_2), 2.85 (6H, s, NMe_2); δ_C(100 MHz; $CDCl_3$) 149.1 (C-1, C-3), 146.5 (ArCH*C*HNMe_2), 129.1 (C-2), 127.2 (C-4, C-6), 122.4 (C-5), 83.5 (Ar*C*HCHNMe_2), 40.5 (NMe_2); ν_{max}(neat)/cm^{-1} 2899, 1625, 1594, 1519, 1442, 1417, 1382, 1346, 1280, 1217, 1100, 958, 920, 879, 847, 771, 734, 707; *m/z* (EI) 237.07489 (M^+, $C_{10}H_{11}N_3O_4$ requires 237.07496).

***trans*-6-[β-(Dimethylamino)vinyl]-5-nitroquinoline (29)**

Brilliant red crystals, 90% yield, R_f = 0.37 (light petroleum : Et_2O = 9 : 1); mp 175 °C; (Found: C, 63.83; H, 5.41; N, 17.06 $C_{13}H_{13}N_3O_2$ requires C, 64.19; H, 5.39; N, 17.27%); δ_H(600 MHz; $CDCl_3$) 8.71 (1H, d, *J* 9 Hz, H-2), 7.92 (2H, d, *J* 9 Hz, H-4, H-8), 7.71 (1H, d, *J* 9 Hz, H-7), 7.37 (1H, m, H-3), 7.06 (1H, d, *J* 14 Hz, ArCHC*H*NMe_2), 5.20 (1H, d, *J* 14 Hz, ArC*H*CHNMe_2), 2.70 (6H, s, NMe_2); δ_C(150 MHz; $CDCl_3$) 148.3 (C-2), 145.2 (ArCH*C*HNMe_2), 144.6 (C-8′), 140.1 (C-6), 131.6 (C-8), 131.47 (C-5), 128.8 (C-4), 124.7 (C-7), 122.9 (C-3), 121.7 (C-4′), 88.3 (Ar*C*HCHNMe_2), 40.5 (NMe_2); ν_{max}(neat)/cm^{-1} 2895, 1632, 1614, 1512, 1432, 1360, 1206, 1164, 1137, 1103, 926, 873, 818, 797, 778, 728; *m/z* (EI) 243.10033 (M^+, $C_{13}H_{13}N_3O_2$ requires 243.10078); 243.1 (25%) (M^+), 131.0 (70%), 119.0 (50%).

***trans*-7-[β-(Dimethylamino)vinyl]-8-nitroquinoline (31)** [33]

Lustrous red crystals, 92% yield, R_f = 0.46 (light petroleum : Et_2O = 9 : 1); mp 180 °C (lit. mp 181–183 °C);[33] (Found: C, 63.91; H, 5.45; N, 17.13 $C_{13}H_{13}N_3O_2$ requires C, 64.19; H, 5.39; N, 17.27%); δ_H(400 MHz; $CDCl_3$) 8.77 (1H, d, *J* 8 Hz, H-2), 7.95 (1H, d, *J* 8 Hz, H-4), 7.49 (2H, m, H-5, H-6), 7.24 (1H, m, H-3); 7.03 (1H, d, *J*14 Hz, ArCHC*H*NMe_2), 4.99 (1H, d, *J* 14 Hz, ArC*H*CHNMe_2), 2.87 (6H, s, NMe_2); δ_C(100 MHz; $CDCl_3$) 151.6 (C-2), 144.9 (ArCH*C*HNMe_2), 142.4 (C-7), 141.1 (C-8′), 135.3 (C-4), 132.6 (C-8), 128.5 (C-5), 124.5 (C-4′), 121.9 (C-6), 120.0 (C-3), 88.1 (Ar*C*HCHNMe_2), 40.6 (NMe_2); ν_{max}(neat)/cm^{-1}2912, 1633, 1607, 1516, 1366, 1306, 1269, 1200, 1105, 870, 824, 760; *m/z* (EI) 243.10059 (M^+, $C_{13}H_{13}N_3O_2$ requires 243.10078), 243.1 (40%) (M^+), 226.1 (25%), 142.1 (25%).

2,6-Bis-*trans*-[β-(dimethylamino)vinyl]-3-nitropyridine (33)

Deep red crystals, 95% yield, R_f = 0.4 (100% ether); mp 131 °C; (Found: C, 59.26, H, 6.70, N, 21.32 $C_{13}H_{18}N_4O_2$ requires C, 59.53, H, 6.92, N, 21.36%); δ_H(400 MHz; $CDCl_3$) 7.96 (1H, d, *J* 14 Hz, H-4), 7.94 (1H, d, *J* 9 Hz, C-2-CHC*H*NMe_2), 7.52 (1H, d, *J* 14 Hz, C-6-CHC*H*NMe_2), 6.36 (1H, d, *J* 14 Hz, C-2-C*H*CHNMe_2), 6.32 (1H, d, *J* 9 Hz, H-5), 5.04 (1H, d, *J* 14 Hz, C-6-C*H*CHNMe_2), 2.94 (6H, s, NMe_2), 2.89 (6H, s, NMe_2); δ_C(100 MHz; $CDCl_3$) 162.4 (NMe_2), 161.5 (C-6), 153.7 (C-2), 150.0 (C-2-CH*C*HNMe_2), 147.4 (C-6-CH*C*HNMe_2), 134.0 (C-4), 133.2 (C-3), 112.4 (C-5), 96.0 (C-6-*C*HCHNMe_2), 93.0 (C-2-*C*HCHNMe_2), 40.9 (NMe_2), 36.4 (NMe_2), 31.3 (NMe_2); ν_{max}(neat)/cm^{-1} 2877, 1613, 1533, 1357, 1253, 1225, 1093, 1069, 825, 793; *m/z* (EI) 262.1440 (M^+, $C_{13}H_{18}N_4O_2$ requires 262.1430), 262.1 (13%) (M^+), 181.0 (30%), 131.0 (40%).

***trans*-2-[β-(Dimethylamino)vinyl]-nitronaphthalene (37)** [33]

Dark red crystals, 85% yield, R_f = 0.48 (CH_2Cl_2 : Et_2O = 1 : 1); mp 101 °C (lit. mp 98–110 °C);[33] (Found: C, 69.52, H, 5.97, N, 11.58 $C_{14}H_{14}N_2O_2$ requires C, 69.41, H, 5.82, N, 11.56%); δ_H(600 MHz; $CDCl_3$) 7.70 (1H, d, *J* 8 Hz, ArH), 7.66 (1H, d, *J* 8 Hz, ArH), 7.58 (1H, d, *J* 8 Hz, ArH), 7.48 (2H, m, ArH), 7.32 (1H, m, ArH), 6.97 (1H, d, *J* 14 Hz, ArCHC*H*NMe_2), 5.11 (1H, d, *J* 14 Hz, ArC*H*CHNMe_2), 2.86 (6H, s, NMe_2), δ_C(150 MHz; $CDCl_3$) 144.4, 142.3, 130.0, 128.3, 127.8, 125.8, 124.8, 121.3, 120.4, 88.7, 40.5; ν_{max}(neat)/cm^{-1} 2933, 1634, 1614, 1514, 1377, 1265, 1030, 814, 734, 637; *m/z* (+ESI) 265.0953 (M + Na, $C_{14}H_{14}N_2O_2Na$ requires 265.0953).

General procedure for the catalytic hydrogenation of nitroenamines to the corresponding indole derivatives

To a stirred suspension of Pd/C (10 wt%) (0.14 g, 0.13 mmol) in MeOH (40 mL) was added a solution of *trans*-2-[β-(dimethylamino)vinyl]-2-nitrobenzene (0.25 g, 1.30 mmol) in CH_2Cl_2 (5 mL). For compounds **29**, **31**, **33** and **35**, acetic acid

(2.5 mL) was added to prevent catalyst poisoning. The solution was then saturated with H_2 gas and stirred overnight under H_2 at room temperature. The reaction mixture was then purged with Ar and the Pd/C was filtered through a short pad of celite before washing with EtOAc (15 mL). The filtrate was concentrated (1 mL) and purified by passing through a bond elut silica cartridge[18] followed by elution with EtOAc (2 × 30 mL). The combined filtrates were then concentrated and recrystallised.

Indole (40)[34]

Colourless prisms, 75% yield, R_f = 0.61 (light petroleum : CH_2Cl_2 = 1 : 1); mp 53 °C (lit. mp 52–54 °C);[34] (Found: C, 82.30, H, 6.24, N, 12.02 C_8H_7N requires C, 82.02, H, 6.02, N, 11.96%); δ_H(400 MHz; $CDCl_3$) 8.02 (1H, bs, N*H*), 7.80 (1H, d, *J* 7 Hz, H-4), 7.40 (1H, d, *J* 7 Hz, H-7), 7.35 (1H, t, *J* 7 Hz, H-6), 7.28 (1H, t, *J* 7 Hz, H-5), 7.17 (1H, bd, H-2), 6.68 (1H, bd, H-3); δ_C(100 MHz; $CDCl_3$) 135.9 (C-7′), 128.0 (C-3′), 124.4 (C-2), 122.1 (C-5), 120.8 (C-4), 119.9 (C-6), 111.3 (C-7), 102.5 (C-3); ν_{max}(neat)/cm^{-1} 3405, 1454, 1413, 1334, 1245, 1091, 907, 740, 723; *m*/*z* (EI) 117.05736 (M^+, C_8H_7N requires 117.05785), 130.1 (10%), 117.1 (52%) (M^+), 90.0 (80%), 63 (100%).

Methyl indole-4-carboxylate (41)[35]

Off white solid, 65% yield, R_f = 0.62 (light petroleum : EtOAc = 1 : 1); mp 64 °C (lit. mp 63–65 °C);[35] (Found: C, 68.64, H, 5.31, N, 7.82 $C_{10}H_9NO_2$ requires C, 68.56, H, 5.18, N, 8.00%); δ_H(400 MHz; $CDCl_3$) 9.16 (1H, bs, N*H*), 7.92 (1H, d, *J* 7 Hz, H-5), 7.55 (1H, d, *J* 7 Hz, H-7), 7.29 (1H, m, H-6), 7.20 (1H, bd, H-2), 7.18 (1H, bd, H-3), 3.98 (3H, s, OMe); δ_C(100 MHz; $CDCl_3$) 168.5 (C=O), 136.8 (C-7′), 127.4 (C-3′), 126.7 (C-6), 123.3 (C-5), 121.3 (C-4), 120.9 (C-2), 116.3 (C-7), 103.4 (C-3), 51.8 (OMe); ν_{max}(neat)/cm^{-1}3346, 1697, 1273, 1192, 1142, 909, 898, 753, 731; *m*/*z* (EI) 175.06353 (M^+, $C_{10}H_9NO_2$ requires 175.06333), 175.1 (70%) (M^+), 144.0 (92%), 116.1 (70%), 68.9 (70%).

4-Fluoroindole (42)[36]

Colourless crystals, 60% yield, R_f = 0.74 (light petroleum : CH_2Cl_2 = 1 : 1); mp 26 °C (lit. mp 25–28 °C);[36] (Found: C, 70.98, H, 4.67, N, 10.21 C_8H_6NF requires C, 71.10, H, 4.48, N, 10.36%); δ_H(400 MHz; $CDCl_3$) 8.26 (1H, bs, N*H*), 7.21–7.13 (3H, m, H-2, H-6, H-7), 6.81 (1H, m, H-5), 6.67 (1H, bd, H-3); δ_C(100 MHz; $CDCl_3$) 155.3 (J_{C-F} 246 Hz, C-4), 138.5 (J_{C-F} 11 Hz, C-7′), 124.1 (C-2), 122.5 (J_{C-F} 11 Hz, C-6), 117.0 (J_{C-F} 21 Hz, C-3′), 107.1 (C-7), 104.4 (J_{C-F} 21 Hz, C-5), 98.7 (C-3); ν_{max}(neat)/cm^{-1} 3421, 1579, 1501, 1353, 1225, 1078, 1012, 738, 670; *m*/*z* (EI) 135.04913 (M^+ C_8H_6NF requires 135.04843), 135 (70%) (M^+), 119 (45%), 68.9 (100%).

4-Bromoindole (43)[23a]

Colourless oil, 67% yield, R_f = 0.55 (light petroleum : CH_2Cl_2 = 3 : 2); (Found: C, 49.29, H, 3.21, N, 7.18 C_8H_6NBr requires C, 49.01, H, 3.08, N, 7.14%); δ_H(600 MHz; $CDCl_3$) 8.26 (1H, bs, N*H*), 7.33 (1H, d, *J* 8 Hz, H-7), 7.30 (1H, d, *J* 8 Hz, H-5), 7.24 (1H, t, *J* 3 Hz, H-2), 7.06 (1H, t, *J* 8 Hz, H-6), 6.63 (1H, t, *J* 3 Hz, H-3); δ_C(150 MHz; $CDCl_3$) 136.0 (C-7′), 128.7 (C-3′), 124.7 (C-2), 122.9 (C-6), 122.8 (C-5), 114.8 (C-4), 110.2 (C-7), 103.1 (C-3); ν_{max}(neat)/cm^{-1} 3419, 1564, 1428, 1332, 1177, 889, 743; *m*/*z* (EI) 194.96849 (M^+, C_8H_6NBr requires 194.96836), 197 (92%), 195 (93%) (M^+).

4-Methoxyindole (44)[37]

Off-white crystals, 63% yield, R_f = 0.41 (light petroleum : CH_2Cl_2 = 1 : 1); mp 68 °C (lit. mp 68–69 °C);[37] (Found: C, 73.43; H, 6.16; N, 9.51. C_9H_9NO requires C, 73.45; H, 6.16; N, 9.51%); δ_H(600 MHz; $CDCl_3$) 8.13 (1H, bs, N*H*), 7.15 (1H, t, *J* 8 Hz, H-6), 7.09 (1H, m, H-7), 6.94 (1H, d, *J* 8 Hz, H-2), 6.72 (1H, bd, H-5), 6.38 (1H, d, *J* 8 Hz, H-3), 4.00 (3H, s, OMe); δ_C(100 MHz; $CDCl_3$) 153.4 (C-4), 137.3 (C-7′), 122.8 (C-6, C-7), 118.6 (C-3′), 104.6 (C-2), 99.8 (C-3, C-5), 55.4 (OMe); ν_{max}(neat)/ cm^{-1} 3381, 1615, 1586, 1507, 1497, 1350, 1281, 1242, 1078, 1054, 961, 744, 726; *m*/*z* (EI) 147.06774 (M^+, C_9H_9NO requires 147.17390), 147.1 (100%) (M^+), 132.0 (100%), 116.0 (20%), 104.1 (80%), 83.0 (30%).

4-Chloroindole (45)[38]

Light pink oil, 74% yield, R_f = 0.38 (light petroleum : CH_2Cl_2 = 4 : 1); (Found: C, 63.59, H, 4.15, N, 9.16 C_8H_6NCl requires C, 63.38, H, 3.99, N, 9.24%); δ_H(600 MHz; $CDCl_3$) 8.13 (1H, bs, N*H*), 7.29 (1H, t, *J* 7 Hz, H-7), 7.24 (1H, t, *J* 3 Hz, H-2), 7.13 (2H, m, H-6, H-5), 6.67 (1H, t, *J* 3 Hz, H-3); δ_C(150 MHz; $CDCl_3$) 136.5 (C-7′), 126.8 (C-3′), 126.1 (C-4), 124.7 (C-2), 122.6 (C-5), 119.6 (C-6), 109.6 (C-7), 101.4 (C-3); ν_{max}(neat)/ cm^{-1} 3421, 1571, 1485, 1432, 1338, 1182, 928, 745; *m*/*z* (EI) 151.01852 (M^+, C_8H_6NCl requires 151.01888), 153 (55%), 151.1 (50%) (M^+), 116.1 (30%), 89.1 (42%).

6-Bromoindole (46)[23b–d]

Off-white solid, 52% yield, mp 94 °C (lit. mp 95–96 °C);[23b] δ_H(600 MHz; $CDCl_3$) 8.15 (1H, bs, N*H*), 7.55 (1H, d, *J* 2 Hz, H-7), 7.53 (1H, d, *J* 9 Hz, H-4), 7.24 (1H, dd, *J* 2 Hz, 9 Hz, H-5), 7.19 (1H, t, *J* 3 Hz, H-2), 6.61 (1H, m, H-3); ^{1}H NMR data was in agreement to the literature assignments.

1*H*-Benz[*g*]indole (47)[39]

Off-white solid; 90% yield, R_f = 0.41 (light petroleum : EtOAc = 4 : 1); mp 178 °C (lit. mp 179 °C);[39] (Found: C, 86.04, H, 5.52, N, 8.42 $C_{12}H_9N$ requires C, 86.20, H, 5.43, N, 8.38%); δ_H(400 MHz; $CDCl_3$) 8.79 (1H, bs, N*H*), 7.93 (2H, d, ArH), 7.75 (1H, d, ArH), 7.44 (3H, d, ArH), 7.24 (1H, m, ArH), 6.73 (1H, m, ArH); δ_C(100 MHz; $CDCl_3$) 130.5, 128.9 (CH), 125.5 (CH), 123.9 (CH), 122.3 (CH), 120.8 (CH), 120.7 (CH), 119.3 (CH), 104.3 (CH); ν_{max}(neat)/cm^{-1} 3412, 1494, 1379, 1110, 1078, 809, 719, 687; *m*/*z* (EI) 167.07290 (M^+, $C_{12}H_9N$ requires 167.07350), 167.1 (50%) (M^+).

1*H*-Pyrrole[2,3-*f*]quinoline (48)[40]

Light tan solid, 80% yield, R_f = 0.7 (EtOAc : MeOH = 4 :1); mp 224 °C (lit. mp 222–224 °C);[40] (Found: C, 78.03, H, 7.79, N, 16.39 $C_{11}H_8N_2$ requires C, 77.96, H, 8.05, N, 16.66%); δ_H(600 MHz; CD_3OD) 12.55 (1H, bs, N*H*), 9.90 (1H, d, *J* 7 Hz, H-7), 8.97 (1H, d, *J* 7 Hz, H-9), 8.32 (1H, d, *J* 7 Hz, H-4), 8.03 (1H, m, H-8), 7.73 (1H, m, H-5), 7.69 (1H, bd, H-2), 6.78 (1H, bd, H-3); δ_C(100 MHz; CD_3OD) 139.7 (C-7), 139.9 (C-9), 136.0 (C-5′), 131.2 (C-4), 127.5 (C-2), 123.3 (C-3′), 121.9 (C-9″), 120.2 (C-8), 118.3 (C-9′), 110.2 (C-5), 99.8 (C-3); ν_{max}(neat)/ cm^{-1} 2658, 1587, 1345, 1267, 877, 812, 736, 720, 678; *m*/*z* (EI) 168.06849 (M^+, $C_{11}H_8N_2$ requires 168.06875) 168.1 (100%) (M^+), 140.1 (30%), 100.0 (32%).

1*H*-Pyrrole[3,2-*h*]quinoline (49)[12a]

Pale green solid, 75% yield, R_f = 0.58 (light petroleum : EtOAc = 1 : 9); mp 100 °C (lit. mp 99–101 °C);[12a] (Found: C, 78.09, H, 7.94, N, 16.45 $C_{11}H_8N_2$ requires C, 77.96, H, 8.05, N, 16.66%); δ_H(400 MHz; $CDCl_3$) 13.03 (1H, bs, N*H*), 8.77 (1H, d, *J* 7 Hz, H-8), 8.74 (1H, bd, H-6), 8.04 (1H, d, *J* 8 Hz, H-2), 7.70 (2H, s, H-4, H-5), 7.61 (1H, d, *J* 8 Hz, H-7), 6.83 (1H, bd, H-3); δ_C(100 MHz; $CDCl_3$) 145.0 (C-8), 138.2 (C-6), 131.8 (C-9′), 129.6 (C-2), 129.5 (C-3′), 126.5 (C-5′), 125.9 (C-5), 123.0 (C-9″), 118.8 (C-4), 117.6 (C-7), 105.1 (C-3); ν_{max}(neat)/cm^{-1} 3047, 2336, 1534, 1392, 1375, 1213, 794, 742, 710, 676; *m*/*z* (EI) 168.06813 (M^+, $C_{11}H_8N_2$ requires 168.06875), 168.1 (60%) (M^+), 155.0 (40%), 91 (100%).

5-(*N*,*N*-dimethylaminoethyl)-4-azaindole (50)

Pale yellow solid, 70% yield, R_f = 0.4 (EtOAc : MeOH = 9 : 1); mp 174–175 °C; (Found: C, 70.04, H, 8.10, N, 22.27 $C_{11}H_{15}N_3$ requires C, 69.81, H, 7.99, N, 22.20%); δ_H(400 MHz; CD_3OD) 8.20 (1H, d, *J* 9 Hz, H-7), 7.96 (1H, bd, H-2), 7.53 (1H, d, *J* 9 Hz, H-6), 6.90 (1H, bd, H-3), 3.94 (2H, m, $ArCH_2CH_2NMe_2$), 3.64 (2H, m, $ArCH_2CH_2NMe_2$), 3.08 (6H, s, NMe_2); δ_C(100 MHz; CD_3OD) 148.6 (C-5), 145.2 (C-3′), 129.9 (C-2), 128.2 (C-7′), 120.7 (C-7), 116.3 (C-6), 101.2 (C-3), 57.8 ($ArCH_2CH_2NMe_2$), 43.0 (NMe_2), 34.7 (NMe_2), 30.9 ($ArCH_2CH_2NMe_2$); ν_{max}(neat)/cm^{-1} 3363, 2964, 2760, 1613, 1570, 1467, 1409, 1022, 890, 791, 744; *m*/*z* (EI) 189.12675 (M^+, $C_{11}H_{15}N_3$ requires 189.12660) 189.1 (21%) (M^+), 145.1 (20%), 118.1 (18%).

Ethyl 5-(*N*,*N*-dimethylamino)-6-cyano-4-azaindole-7-carboxylate (51)

Yellow solid, 63% yield, R_f = 0.33 (light petroleum : EtOAc = 7 : 3); mp 150 °C; (Found: C, 61.19, H, 6.54, N, 20.12 $C_{13}H_{14}N_4O_4$ requires C, 61.30, H, 6.61, N, 20.42%); δ_H(400 MHz; $CDCl_3$) 9.60 (1H, bs, N*H*), 7.61 (1H, m, H-3), 6.60 (1H, m, H-2), 4.54 (2H, q, *J* 7 Hz, CH_2CH_3), 3.14 (6H, s, NMe_2), 1.53 (3H, t, *J* 7 Hz, CH_2CH_3); δ_C(100 MHz; $CDCl_3$) 164.5 (C=O), 161.4 (C-5), 149.0 (C-3′), 133.5 (C-3), 123.0 (C-7′), 117.5 (C≡N), 115.4 (C-6), 103.1 (C-2), 90.2 (C-7), 62.8 (CH_2CH_3), 42.7 (NMe_2), 14.0 (CH_2CH_3); ν_{max}(neat)/cm^{-1} 3313, 2935, 1725, 1605, 1412, 1382, 1269, 1114, 1024, 876, 789; *m*/*z* (+ESI) 281.1012 (M^+, $C_{13}H_{14}N_4O_4$ requires 281.1014) 206.1 (40%), 231.1 (30%), 259.1 (28%).

Transfer hydrogenation of enamines to the corresponding indoles using Pd-EnCat™/HCOOH/Et_3N[25b]

trans-2-[β-(Dimethylamino)vinyl]-nitronaphthalene **37** (70 mg, 0.29 mmol., 1 eq.) was dissolved in anhydrous EtOAc (5 mL). To the solution was added, catalyst Pd-EnCat™ (loading 0.4 mmol g^{-1}) (43.58 mg, 0.017 mmol., 6 mol%) followed by Et_3N (0.203 mL, 147 mg, 1.45 mmol., 5 eq.) and HCOOH (0.06 mL, 67 mg, 1.45 mmol., 5 eq.). The mixture was stirred at room temperature for 24 h. The reaction was monitored by TLC and LCMS. Pd-EnCat™ catalyst was removed by filtration, and the filtrate was washed with saturated NH_4Cl solution (3 × 10 mL). The organic solution was dried over Na_2SO_4, before concentrating under reduced pressure. Filtration of the crude material through a bond elut silica cartridge and recrystallisation from CH_2Cl_2/light petroleum (1 : 3) gave the corresponding indole, *1H*-benz[*g*]indole **47**, (48.5 mg, 78%) as an off-white solid. ^{1}H NMR was in agreement with the previously prepared sample.

Microwave-assisted transfer hydrogenation of enamines to the corresponding indoles using Pd-EnCat™/HCOOH/Et_3N

To a solution of *trans*-2-[β-(dimethylamino)vinyl]-nitronaphthalene**37** (40 mg, 0.165 mmol., 1 eq.) dissolved in anhydrous EtOAc (3 mL) was added Pd-EnCat™ catalyst (0.4 mmol g^{-1}) (41.2 mg, 0.017 mmol., 10 mol%) followed by Et_3N (0.115 mL, 83 mg, 0.82 mmol., 5 eq.) and HCOOH (0.311 mL, 38 mg, 0.82 mmol., 5 eq.). The mixture was heated in the Emrys Liberator™ for 2 h at 120 °C.[16] Pd-EnCat™ catalyst was removed by filtration, and the filtrate was washed with saturated NH_4Cl solution (3 × 10 mL). The organic solution was dried over Na_2SO_4 before concentrating under reduced pressure. Filtration of the crude material through a bond elut silica cartridge and recrystallisation from CH_2Cl_2/light petroleum (1 : 3) gave the corresponding indole, 1*H*-benz[*g*]indole **47**, (18 mg, 68%) as an off-white solid. ^{1}H NMR was in agreement with the previously prepared sample.

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