Sonogashira Cross-Coupling Reactions and Construction of the Indole Ring System Using a Robust, Silica-Supported Palladium Catalyst

Elizabeth Tyrrell,* Leon Whiteman, Neil Williams

School of Pharmacy and Chemistry, Kingston University, Penrhyn Road, Kingston upon Thames, Surrey, KT1 2EE, UK
Fax +44(208)5477562; E-mail: e.tyrrell@kingston.ac.uk

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Abstract: The use of a recyclable silica-supported palladium catalyst in Sonogashira couplings and indole syntheses using a range of functionalised substrates is described. The catalyst is shown to be both robust and versatile, effecting the synthesis of 2-phenylindole in quantitative yield without the need for N-protection, a copper co-catalyst, a base, or a solvent.

Key words: Sonogashira cross-coupling, silica-supported catalysis, palladium catalyst, indoles, enynes

Immobilising transition metal catalysts onto solid supports for use in synthesis has received significant attention in recent years.[1] This has been driven by growing interest in attempts to create environmentally friendly chemical processes. Coupled with this are the benefits of recycling valuable resources and the ease of separating the catalyst from reaction mixtures by filtration.

Many supported transition metal complexes have found application in cross-coupling reactions, and of interest to us was the recent use of a polystyrene-supported palladium catalyst in Sonogashira reactions using aryl iodides.[2] High yields were obtained and the recyclability of the complex was demonstrated; however, a copper cocatalyst was required as well as a suitable solvent to pre-swell the polystyrene support. The results of our attempts at the Sonogashira coupling reaction, using a silica-supported catalyst, were disseminated shortly afterwards,[3] in which we demonstrated the efficacy of the catalyst using both copper-free and solvent-free experimental conditions.

Since then others have contributed to this field. A versatile pyridyl-functionalised silica-supported catalyst has been reported to be capable of effecting Sonogashira couplings, Heck reactions, and cyanation reactions, all in high yields and with good recyclability.[4,5] Notably, aryl bromides were reactive in these studies. Macquarrie et al. have reported numerous solid-supported catalyst systems including an N,N-chelated silica-supported palladium catalyst for high-yielding Sonogshira reactions[6] and asymmetric hydrogenation reactions using silica-supported ferrocenylphosphine ligands.[7] A polystyrene-supported N-heterocyclic carbene (NHC) palladium catalyst, capable of coupling aryl iodides and activated aryl bromides in good yields and under copper-free Sonogashira conditions[8] has also contributed to this area of catalysis. Recent publications by Cai et al. described highly recyclable, silica-supported thioether[9] and phosphine[10] palladium complexes capable of high-yielding Sonogashira reactions.

Another application for immobilised catalysts is in the synthesis of structural motifs found in nature. The indole nucleus has been constructed via an intramolecular cyclisation of 2-(phenylethynyl)aniline derivatives.[11] This research group used palladium on carbon and copper iodide in a one-pot Sonogashira coupling/heteroannulation reaction (the product, 2-phenylindole, was isolated in 72% yield). The same group then went on to use a supported bimetallic (Pd–Cu) complex for the same sequence of reactions with excellent results[12] (up to 100% conversion was observed). Often, to facilitate the cyclisation reaction, the amino-bearing substrate may be derivatised by *N*-methylsulfonylation, for example.[13] In the presence of copper(II) trifluoroacetate, the cyclisation product was obtained in 99% yield. This catalyst system was shown to be recyclable; however, the underivatised substrate proved to be unreactive. In an analogous study, Palimkar et al., using both *N*-tosyl and *N*-mesyl substrates, in combination with palladium(II) acetate and ultrasonic irradiation, were able to obtain good yields without the need of a copper source.[14] Wu et al. used a one-pot Sonogashira coupling/heteroannulation in a recent indolylquinolinone synthesis;[15] however, stoichiometric amounts of copper cocatalyst were required.

To the best of our knowledge, no methods for the palladium-assisted cyclisation of underivatised (phenylethynyl)aniline substrates under copper-free conditions have been described.

In an earlier communication[3] we described one of the first applications of silica-supported palladium catalyst **1** in Sonogashira coupling reactions (Scheme 1). In our preliminary coupling investigations using simple, nonfunctionalised aryl iodides and alkynes we found that the reaction could be conducted in the absence of a copper co-catalyst with piperidine (threefold excess) serving a dual role of base and solvent (Scheme 1).

In these examples the couplings were rapid and highly efficient. The use of a silica support avoids the need for preswelling in solvent and allows for straightforward recovery and recycling of the catalyst, further emphasising the environmentally benign nature of the process. Since copper is known to promote alkyne–alkyne homocoupling (the Glaser reaction),[16] the copper-free process presents it-

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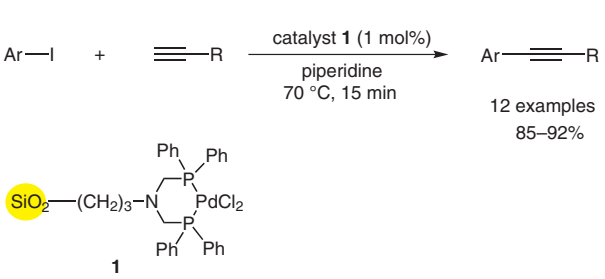
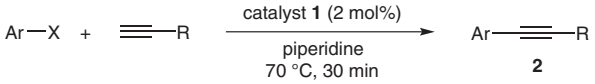


Scheme 1 Our previously reported Sonogashira couplings using silica-supported palladium catalyst **1**

self as a more selective reaction. We present here the results of a more extensive study into the utility of catalyst **1**, in which we explored its tolerance to a range of functional moieties present in both the alkyne and the halide substrates, and its use in heteroannulation reactions.

The results of Sonogashira couplings (Scheme 2) using a range of functionalised substrates with differing electronic and steric properties to produce alkynes **2** are summarised in Table 1.



Scheme 2 Sonogashira coupling reactions

Aryl iodides were generally highly reactive, with those 4-substituted with electron-withdrawing groups (Table 1, entries 5 and 8) undergoing rapid and efficient coupling. In contrast to this result, the reaction of the 2-substituted aryl iodide (entry 7) is significantly less efficient (59% yield) than that of the 4-substituted aryl iodide (entry 8) (82% yield). Small amounts of the bis-Sonogashira products [1,2- and 1,4-bis(phenylethynyl)benzene] were also isolated with these substrates. Aryl iodides with electron-donating groups (entries 3 and 6) suffered slower conversion rates and lower yields. In general, catalyst **1** proved to be highly selective for the cross-coupled product, although trace amounts (<1%) of alkyne–alkyne homocoupling products were present in some reaction mixtures (identified by GC-MS).

These data suggest that catalyst **1** is tolerant of increased functionalisation in the substrates, effecting the coupling

Table 1 Investigating the Versatility of Catalyst **1**

Entry	X	Ar	R	**2**	Conversion[a] (%)	Yield[b] (%)
1	I	Ph	Ph	**2a**	>99	88
2	I	Ph	PMP	**2b**	98	80
3	I	2-$H_2NC_6H_4$	Ph	**2c**	78	60
4	I	Ph	2-$H_2NC_6H_4$	**2c**	95	80
5	I	4-AcC_6H_4	Ph	**2d**	>99	81
6	I	2-MeC_6H_4	Ph	**2e**	63	52
7	I	2-BrC_6H_4	Ph	**2f**	65	59[c]
8	I	4-BrC_6H_4	Ph	**2g**	96	82[c]
9	I	Ph	CMe_2NH_2	**2h**	45	34
10	I	2-$H_2NC_6H_4$	2-$H_2NC_6H_4$	**2i**	>99	74
11	I	4-AcC_6H_4	2-$H_2NC_6H_4$	**2j**	>99	82
12	I	2-$H_2NC_6H_4$	PMP	**2k**	85	60
13	I	4-AcC_6H_4	PMP	**2l**	>99	80
14	I	2-H_2N-5-NCC_6H_3	Ph	**2m**	>99	76
15	I	2-H_2N-5-NCC_6H_3	PMP	**2n**	95	65
16	Br[d]	Ph	Ph	**2a**	32	10
17	Br[d]	4-$O_2NC_6H_4$	Ph	**2o**	89	30[e]
18	Br[d]	4-AcC_6H_4	Ph	**2d**	40	17

[a] The conversion of the halide substrate was determined by GC.
[b] Yield of product isolated after column chromatography.
[c] The bis-coupling product was also isolated in ca. 10% yield.
[d] The reaction time was increased to 60 min.
[e] Nucleophilic substitution of the halide dominated (see text).

reaction efficiently and with good levels of selectivity (Table 1, entries 10–15). Aryl bromides proved to be much less reactive under these conditions (entries 16–18). The presence of a 4-nitro group on the aryl bromide gave higher conversions of the aryl bromide (entry 17); however, a nucleophilic aromatic '*ipso*' substitution reaction dominated to afford 1-(4-nitrophenyl)piperidine as the major product. Attempted couplings using aryl chlorides were unsuccessful.

Heterocyclic substrates were also investigated (Scheme 3). Under the same reaction conditions as those shown in Scheme 2, heterocyclic halides and alkynes proved to be suitable substrates, with excellent conversions observed throughout (Table 2).

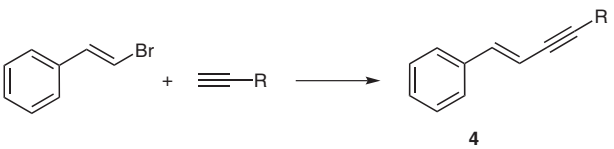
Scheme 3 Heterocyclic Sonogashira coupling reactions

Table 2 Heterocyclic Sonogashira Coupling Reactions

Entry	R^2	R^1	**3**	Conversion[a] (%)	Yield (%)
1	2-thienyl	Ph	**3a**	>99	76
2	3-pyridyl	Ph	**3b**	>99	73
3	5-indolyl	Ph	**3c**	92	76
4	2-thienyl	3-thienyl	**3d**	>99	63
5	2-thienyl	2-$H_2NC_6H_4$	**3e**	95	72
6	2-H_2N-5-ClC_6H_3	3-thienyl	**3f**	95	76
7	5-indolyl	2-$H_2NC_6H_4$	**3g**	96	80

[a] The conversion of the iodide substrate was determined by GC.

To our delight, catalyst **1** also proved to be effective in coupling alkenyl bromides (Scheme 4). In these studies, aromatic alkynes furnished the corresponding enyne products **4** in excellent yields (Table 3, entries 1 and 2). Heterocyclic and non-aromatic alkynes gave enynes **4** in lower, but acceptable yields (entries 3–5).



Scheme 4 Sonogashira coupling of alkenyl bromides

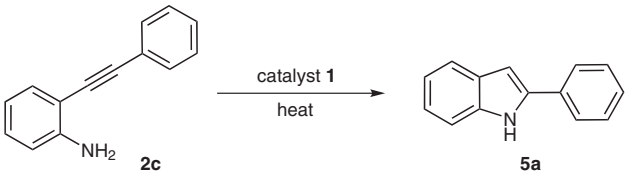
Catalyst **1** could also be recycled. Under the conditions shown in Scheme 1, an initial loading of four mole-percent provided near-quantitative conversions over four consecutive coupling cycles. For each evaluation the catalyst was simply removed from the reaction mixture by filtration, washed with diethyl ether, and dried (in vacuo) before being reused. A significant drop in reaction rate was noted by the fourth cycle, in which a conversion of 95% took place over 72 hours.

Table 3 Sonogashira Coupling Using β-Bromostyrene

Entry	R	**4**	Conversion[a] (%)	Yield (%)
1	Ph	**4a**	98	85
2	2-$H_2NC_6H_4$	**4b**	99	87
3	cyclopentyl	**4c**	77	51
4	3-thienyl	**4d**	95	66
5	TMS	**4e**	81	65

[a] The conversion of the bromide was determined by GC.

Having established the robust nature of catalyst **1** for Sonogashira couplings between functionalized aryl or alkenyl halides and alkynes and that, furthermore, it may be easily recycled, we investigated its application to indole synthesis. Several methods for the palladium-mediated synthesis of 2-substituted indoles have been reported.[11–15] A one-pot Sonogashira cyclisation reaction employed by Gruber et al.[11] appeared attractive; however, in our hands the reaction proceeded slowly (~50% in 48 hours). Additionally, the requirement for a copper cocatalyst, an excess of base, and a solvent medium proved inconsistent with our overall objective of investigating 'greener' synthetic approaches. Much to our delight, we found that exposure of **2c** to catalyst **1** (10 mol%) at 160 °C furnished the corresponding 2-phenylindole (**5a**) in virtually quantitative conversion (Scheme 5; Table 4, entry 1).



Scheme 5 Heteroannulation reaction

The most noteworthy features of this reaction were that it was achieved without recourse to N-protection of **2c**, in the complete absence of a copper cocatalyst, and without the need for any solvent or additional base. Table 2 provides data on an attempted optimisation study. Using an increased amount of catalyst at a slightly elevated temperature of 120 °C (entry 2) provides optimum conversion rates. The same outcome could be achieved by using less catalyst at a lower temperature over a longer duration (entry 10).

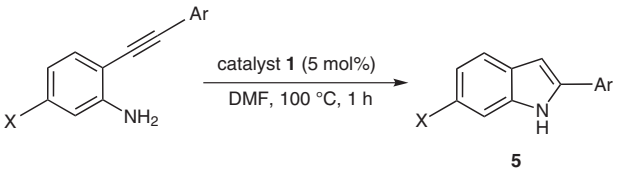
Fortuitously, **2c** proved to be an ideal substrate as it melted on heating and product **5a** (Table 5, entry 1) solidified upon formation (mp 188–190 °C),[17] allowing the reaction to be easily monitored. It is worth noting, however, that

Table 4 Optimisation Studies

Entry	Cat. (mol%)	Temp (°C)	Time (min)	Conversion[a] (%)
1	10	160	20	>99
2	10	120	20	>99
3	10	100	20	96
4	10	90	20	67
5	4	100	20	12
6	4	100	180	68
7	2	100	20	27
8	2	100	60	63
9	5	100	20	77
10	5	100	60	>99

[a] The conversion of **2c** was determined by GC.

the reaction is solvent-free only by virtue of the low melting point of **2c** (mp 89–92 °C). Substrates that are solid at 100 °C do require additional solvent. This has been demonstrated in the cyclisation affording indole **5b** (Scheme 6; Table 5, entry 2).



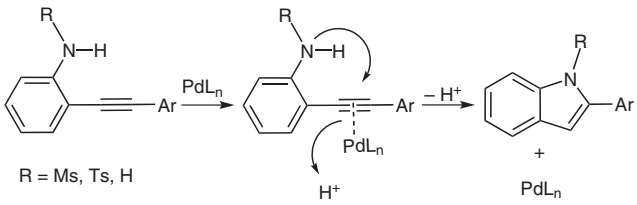
Scheme 6 Cyclisation reactions

Table 5 Indole Synthesis Using Catalyst **1**

Entry	Ar	X	**5**	Conversion[a] (%)	Yield (%)
1	Ph	H	**5a**	>99	96
2	5-indolyl	H	**5b**	>99[b]	91
3	3-thienyl	Cl	**5c**	98[b]	89[c]
4	2-thienyl	H	**5d**	98[b]	90[c]

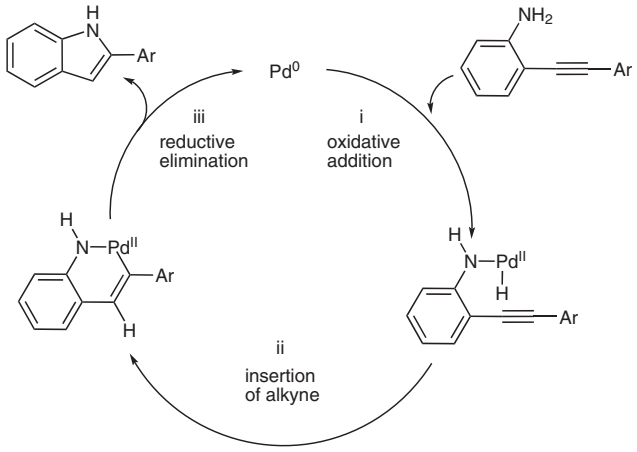
[a] The conversion of the alkyne substrate was determined by GC.
[b] DMF (1 mL) was used as solvent.
[c] The reaction time was increased to 90 min.

This indole synthesis occurred in near-quantitative conversion when *N*,*N*-dimethylformamide (1 mL) was used as solvent. That this reaction is so highly efficient in the absence of a base or cocatalyst raises questions about the mechanism of this '5-*endo*-dig' process. Some suggestions that have appeared in the literature are summarised in Scheme 7.[15,18]



Scheme 7 Reported mechanism for indole formation[15,18]

The reported mechanisms involve the initial coordination of the alkyne to the metal centre followed by nucleophilic attack by the nitrogen atom and proton transfer. In the absence of a copper source and external base, we would tentatively suggest the mechanism shown in Scheme 8. Following formation of the active palladium(0) catalyst, cyclisation is expected to proceed via oxidative addition of the N–H bond (i), which is a somewhat uncommon process, although examples do exist in the literature.[19,20] This is followed by insertion of the alkyne into the Pd–H bond (ii) yielding a palladacyclic intermediate (similar species have previously been isolated and characterised[21]). Finally, reductive elimination (iii) of the palladacycle would yield the expected product.



Scheme 8 Postulated mechanism for indole formation

From our preliminary investigations into the synthetic utility of catalyst **1** in Sonogashira reactions, we have now established its applications using a more diverse range of substrates. We have also demonstrated that the catalyst may be used in reactions with alkenyl bromides and that it may be recycled. The versatile nature of our silica-supported catalyst has been further exemplified in heteroannulation reactions. This proved to be a highly efficient catalyst for this reaction, which occurs in the absence of N-protection, a copper cocatalyst, a base, and, in one example, the absence of solvent. Further studies into this potentially useful process are underway and results will be published in due course.

All NMR spectra were recorded at 400 MHz (^{1}H) and 100 MHz (^{13}C) on a Jeol Eclipse$^+$ 400 NMR spectrometer using Jeol Delta version 4.3.6 control and processing software, copyright 1990–2006, Jeol USA Inc. Chemical shifts are referenced to residual solvent peaks (acetone or $CHCl_3$). Mass spectra were recorded on a Varian CP-3800 gas chromatograph with a Varian 1200L Quadrupole mass spectrometer controlled with Varian Saturn GC/MS system control version 6.41, copyright 1989–2004, Varian Inc. Melting point determinations were carried out on a Stuart Scientific SMP3 digital melting point apparatus and are uncorrected.

Catalyst 1[2]

All solvents used were freshly distilled and all manipulations were carried out under an atmosphere of N_2. 3-Aminopropyl-functionalised silica (2.36 g, 2.36 mmol) was dried over P_2O_5 at 80 °C for 48 h, then suspended in toluene and degassed by sonication (30 min) and N_2 flow overnight. In a separate vessel, paraformaldehyde (0.28 g, 9.44 mmol) was suspended in MeOH (25 mL) and the mixture was refluxed for 2 h. Then Ph_2PH (1.73 mL, 9.44 mmol) was added and the mixture was heated at 90 °C for 44 h. The solvent was removed from the mixture (now a colourless soln) and the resulting clear viscous oil was added to the silica suspension. This mixture was refluxed (130 °C oil bath temperature) with a Dean–Stark trap for 24 h. The resulting mixture was filtered under N_2 and washed sequentially with toluene (2 × 50 mL), CH_2Cl_2 (2 × 50 mL), and again with toluene (2 × 50 mL), and dried in vacuo to yield a pale yellow solid (2.87 g). This solid was reacted with $[PdCl_2(NCPh)_2]$ (0.93 g, 2.4 mmol) in $CHCl_3$ (30 mL) at 60 °C for 24 h. This mixture was filtered and washed with CH_2Cl_2 (3 × 100 mL), Et_2O (3 × 50 mL), THF (3 × 50 mL), and finally CH_2Cl_2 again (3 × 50 mL). Finally, the resulting brown solid (3.16 g) was dried in vacuo overnight.

^{31}P NMR (121 MHz, solid state, ref. to 85% H_3PO_5): δ = 10.35 (s).[2]

Coupling of Aryl Halides and Alkynes; General Procedure[2]

The aryl halide (1 mmol), the alkyne (1.4 mmol), and piperidine (0.297 mL, 3 mmol) were added to a dry Schlenk tube containing catalyst **1** (31.4 mg, 2 mol%). This mixture was heated at 70 °C for 30 min, by which point solidification, due to the presence of a piperidinium salt, had usually occurred. After cooling to r.t., the mixture was diluted with Et_2O (20 mL) and filtered, and the solvent was removed (in vacuo). The crude product was purified by column chromatography (EtOAc–hexane) and recrystallised to yield compounds **2a**–**p**, **3a**–**g**, and **4a**–**e**. The spectral data of all known compounds thus synthesised matched those previously reported and have been referenced where possible.

1,2-Diphenylethyne (2a)

Yield: 157 mg (88%); colourless crystalline solid; mp 60–62 °C (Lit.[10] 59–61 °C).

4-(Phenylethynyl)anisole (2b)

Yield: 166 mg (80%); pale orange solid; mp 65–66 °C (Lit.[10] 56–58 °C).

2-(Phenylethynyl)aniline (2c)

Yield: 154 mg (80%); off-white crystalline solid; mp 89–91 °C (Lit.[25] 87–88 °C).

4-(Phenylethynyl)acetophenone (2d)

Yield: 178 mg (81%); pale yellow crystalline solid; mp 99–103 °C (Lit.[10] 94–96 °C).

2-(Phenylethynyl)toluene (2e)

Yield: 100 mg (52%); colourless oil.[26]

1-(2-Bromophenyl)-2-phenylethyne (2f)

Yield: 151 mg (59%); red/orange oil.[27]

1-(4-Bromophenyl)-2-phenylethyne (2g)

Yield: 210 mg (82%); colourless crystalline solid; mp 80–82 °C (Lit.[22] 82–84 °C).

2-Methyl-4-phenylbut-3-yn-2-amine (2h)

Yield: 54 mg (34%); light brown viscous oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.44 (m, 2 H, ArH), 7.24–7.31 (m, 3 H, ArH), 4.76 (s, 2 H, NH_2), 1.65 (s, 6 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 131.8, 128.4, 128.3, 122.6, 93.2, 82.6, 47.7, 30.7.

MS (EI, 70 eV): *m*/*z* = 159 [M$^+$].

Bis(2-aminophenyl)ethyne (2i)

Yield: 154 mg (74%); light green crystalline solid; mp 154–155 °C (Lit.[29] 154 °C).

4-[(2-Aminophenyl)ethynyl]acetophenone (2j)

Yield: 194 mg (82%); off-white solid; mp 114–116 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 8.60 Hz, 2 H, ArH), 7.60 (d, *J* = 8.60 Hz, 2 H, ArH), 7.36–7.39 (m, 1 H, ArH), 7.15–7.20 (m, 1 H, ArH), 6.71–6.76 (m, 2 H, ArH), 4.30 (s, 2 H, NH_2), 2.62 (s, 3 H, OCH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 217.2, 179.7, 171.9, 136.2, 132.4, 131.6, 130.4, 128.4, 128.3, 118.2, 114.6, 100.0, 94.1, 26.8.

MS (EI, 70 eV): *m*/*z* = 236 [M$^+$].

HRMS (EI): *m*/*z* calcd for $C_{16}H_{14}O_1N_1$: 236.1070; found: 236.1070.

2-[(4-Methoxyphenyl)ethynyl]aniline (2k)

Yield: 142 mg (60%); light orange crystalline solid; mp 99–102 °C (Lit.[34] 104–106 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 (d, *J* = 8.79 Hz, 2 H, ArH), 7.36 (dd, *J* = 1.46 Hz, 1 H, 7.96 Hz, ArH), 7.10–7.16 (m, 1 H, ArH), 6.89 (d, *J* = 8.97 Hz, 2 H, ArH), 6.70–6.76 (m, 2 H, ArH), 4.27 (s, 2 H, NH_2), 3.83 (s, 3 H, OCH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.7, 147.7, 133.0, 132.1, 129.5, 118.0, 115.5, 114.4, 114.1, 108.4, 94.7, 84.5, 55.4.

MS (EI, 70 eV): *m*/*z* = 233 [M$^+$].

4-[(4-Methoxyphenyl)ethynyl]acetophenone (2l)

Yield: 200 mg (80%); pale yellow solid; mp 129–131 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 8.24 Hz, 2 H, ArH), 7.58 (d, *J* = 8.24 Hz, 2 H, ArH), 7.49 (d, *J* = 8.60 Hz, 2 H, ArH), 6.89 (d, *J* = 8.60 Hz, 2 H, ArH), 3.83 (s, 3 H, OCH_3), 2.60 (s, 3 H, $COCH_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.5, 160.2, 136.0, 133.4, 131.5, 128.7, 128.3, 114.5, 93.1, 87.7, 55.3, 26.7.

MS (EI, 70 eV): *m*/*z* = 250 [M$^+$].

4-Amino-3-(phenylethynyl)benzonitrile (2m)

Yield: 175 mg (80%); off-white crystalline solid; mp 88–89 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 1.83 Hz, 1 H, ArH), 7.50–7.55 (m, 2 H, ArH), 7.35–7.40 (m, 4 H, ArH), 6.71 (d, *J* = 8.60 Hz, 1 H, ArH), 4.78 (s, 2 H, NH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.1, 136.4, 133.3, 131.7, 129.0, 128.6, 122.4, 119.5, 114.0, 108.2, 100.2, 96.3, 83.5.

MS (EI, 70 eV): *m*/*z* = 218 [M$^+$].

HRMS (EI): *m*/*z* calcd for $C_{15}H_{10}N_2$: 218.0838; found: 218.0837.

4-Amino-3-[(4-methoxyphenyl)ethynyl]benzonitrile (2n)

Yield: 161 mg (65%); pale-yellow crystalline solid; mp 147–149 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62 (d, *J* = 2.01 Hz, 1 H, ArH), 7.46 (d, *J* = 8.97 Hz, 2 H, ArH), 7.35 (dd, *J* = 8.51 Hz, 1 H, ArH), 6.90 (d, *J* = 8.97 Hz, 2 H, ArH), 6.71 (d, *J* = 8.42 Hz, 1 H, ArH), 4.78 (s, 2 H, NH_2), 3.84 (s, 3 H, OCH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.2, 150.9, 136.2, 133.2, 133.0, 114.4, 114.2, 114.0, 108.7, 100.2, 96.4, 82.1, 55.4.

MS (EI, 70 eV): *m*/*z* = 248 [M$^+$].

HRMS (EI): *m*/*z* calcd for $C_{16}H_{12}O_1N_2$: 248.0944; found: 248.0945.

1-Nitro-4-(phenylethynyl)benzene (2o)
Yield: 67 mg (30%); yellow solid; mp 116–118 °C (Lit.[10] 120–121 °C).

2-(Phenylethynyl)thiophene (3a)
Yield: 140 mg (76%); yellow oil.[23]

3-(Phenylethynyl)pyridine (3b)
Yield: 130 mg (73%); orange crystalline solid; mp 51–53 °C (Lit.[23] 50–51 °C).

5-(Phenylethynyl)indole (3c)
Yield: 165 mg (76%); yellow solid; mp 124–128 °C (Lit.[24] 135 °C).

3-(2-Thienylethynyl)thiophene (3d)
Yield: 110 mg (63%); colourless crystalline solid; mp 97–100 °C.[30]

2-[(2-Aminophenyl)ethynyl]thiophene (3e)
Yield: 143 mg (72%); yellow solid; mp 63–64 °C.[28]

3-[(2-Amino-5-chlorophenyl)ethynyl]thiophene (3f)
Yield: 177 mg (76%); light brown solid; mp 107–110 °C.

^{1}H NMR (400 MHz, acetone-d_6): δ = 7.68–7.72 (m, 1 H, ArH), 7.48–7.51 (m, 1 H, ArH), 7.19–7.24 (m, 2 H, ArH), 6.80 (d, *J* = 2.01 Hz, 1 H, ArH), 6.57 (dd, *J* = 2.01, 8.24 Hz, 1 H, ArH), 5.37 (s, 2 H, NH_2).

^{13}C NMR (100 MHz, acetone-d_6): δ = 150.6, 134.8, 133.1, 129.8, 128.8, 126.0, 122.3, 116.3, 113.4, 105.6, 90.1, 84.6.

MS (EI, 70 eV): *m*/*z* = 233 [M$^+$].

5-[(2-Aminophenyl)ethynyl)]indole (3g)
Yield: 185 mg (80%); pale yellow crystalline solid; mp 183–184 °C.

^{1}H NMR (400 MHz, acetone-d_6): δ = 10.39 (br s, 1 H, indolyl NH), 7.75–7.78 (m, 1 H, ArH), 7.38–7.42 (m, 1 H, ArH), 7.35 (t, *J* = 2.8 Hz, 1 H, ArH), 7.21–7.28 (m, 2 H, ArH), 7.00–7.05 (m, 1 H, ArH), 6.74 (dd, *J* = 0.73, 8.2 Hz, 1 H, ArH), 6.56 (td, *J* = 1.1, 7.4 Hz, 1 H, ArH), 6.45–6.47 (m, 1 H, ArH), 5.04 (s, 2 H, NH_2).

^{13}C NMR (100 MHz, acetone-d_6): δ = 149.2, 136.0, 131.6, 129.1, 128.2, 126.1, 124.8, 123.9, 116.5, 114.0, 113.9, 111.5, 107.8, 101.8, 96.1, 83.5.

MS (EI, 70 eV): *m*/*z* = 232 [M$^+$].

HRMS (EI): *m*/*z* calcd for $C_{16}H_{12}N_2$: 232.0995, found: 232.0995.

β-(Phenylethynyl)styrene (4a)
Yield: 173 mg (85%); colourless crystalline solid; mp 102–103 °C (Lit.[31] 96 °C).

β-[(2-Aminophenyl)ethynyl]styrene (4b)
Yield: 165 mg (87%); dull yellow crystalline solid; mp 111–112 °C.[11]

β-(Cyclopentylethynyl)styrene (4c)
Yield: 100 mg (51%); orange oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23–7.41 (m, 5 H, ArH), 6.88 (d, *J* = 16.29 Hz, 1 H, alkenyl H), 6.19 (dd, *J* = 2.20, 16.29 Hz, 1 H, alkenyl H), 2.75–2.99 (m, 1 H, alkyl H), 1.91–2.06 (m, 3 H, alkyl H), 1.45–1.86 (m, 5 H, alkyl H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.9, 136.7, 128.7, 128.2, 126.1, 109.1, 97.3, 79.4, 34.0, 31.1, 25.1.

MS (EI, 70 eV): *m*/*z* = 196 [M$^+$].

β-(3-Thienylethynyl)styrene (4d)
MP: 89–91 °C.

^{1}H NMR (400 MHz, acetone-d_6): δ = 7.64–7.67 (m, 1 H, ArH), 7.50–7.55 (m, 3 H, ArH), 7.27–7.39 (m, 3 H, ArH), 7.17 (dd, *J* = 1.10 Hz, 1 H, ArH), 7.04 (d, *J* = 16.29 Hz, 1 H, alkenyl H), 6.53 (d, *J* = 16.29 Hz, 1 H, alkenyl H).

^{13}C NMR (100 MHz, acetone-d_6): δ = 141.1, 136.4, 129.6, 128.8, 128.7, 126.4, 126.2, 122.5, 108.0, 88.3, 86.8.

MS (EI, 70 eV): *m*/*z* = 210 [M$^+$].

β-[(Trimethylsilyl)ethynyl]styrene (4e)
Yield: 130 mg (65%); yellow oil.[32]

Cyclisation of 2-(Arylethynyl)aniline Derivatives; General Procedure
A dry Schlenk tube containing the 2-(arylethynyl)aniline derivative (1 mmol), anhyd DMF (1 mL), and catalyst **1** (7.8 mg, 5 mol%) was heated at 100 °C for 60 min, and then the solvent was removed in vacuo. After cooling to r.t., the reaction mixture was chromatographed (silica gel, EtOAc–hexane) to yield the corresponding indole derivative **5**.

2-Phenylindole (5a)
Yield: 185 mg (96%); off-white solid; mp 191–193 °C (Lit.[17] 188–190 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.30 (br s, 1 H, indolyl NH), 7.61–7.70 (m, 3 H, ArH), 7.39–7.48 (m, 3 H, ArH), 7.30–7.35 (m, 1 H, ArH), 7.17–7.23 (m, 1 H, ArH), 7.10–7.15 (m, 1 H, ArH), 6.82–6.85 (m, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.0, 136.9, 132.5, 129.4, 129.1, 127.8, 125.3, 122.5, 120.8, 120.5, 111.0, 100.1.

MS (EI, 70 eV): *m*/*z* = 193 [M$^+$].

HRMS (EI): *m*/*z* calcd for $C_{14}H_{11}N_1$: 193.0886; found: 193.0888.

2-(5-Indolyl)indole (5b)
Yield: 211 mg (91%); light brown solid; mp 146 °C (dec.)

^{1}H NMR (400 MHz, acetone-d_6): δ = 10.50 (br s, 1 H, indolyl NH), 10.28 (br s, 1 H, indolyl NH), 7.97–7.98 (m, 1 H, ArH), 7.56 (dd, *J* = 1.7 Hz, 1.8 Hz, 1 H, ArH), 7.39–7.46 (m, 2 H, ArH), 7.30 (dd, *J* = 0.9, 0.9 Hz, 2 H, ArH), 7.26–7.29 (m, 1 H, ArH), 6.88–6.98 (m, 2 H, ArH), 6.69 (dd, *J* = 0.7, 0.7 Hz, 1 H, ArH), 6.41–6.45 (m, 1 H, ArH).

^{13}C NMR (100 MHz, acetone-d_6): δ = 140.1, 137.4, 136.1, 129.8, 128.6, 125.8, 124.2, 120.9, 119.8, 119.7, 119.4, 116.9, 111.8, 110.9, 102.0, 97.5.

MS (EI, 70 eV): *m*/*z* = 232 [M$^+$].

HRMS (EI): *m*/*z* calcd for $C_{16}H_{12}N_2$: 232.0995; found: 232.0996.

5-Chloro-2-(3-thienyl)indole (5c)
Yield: 208 mg (89%); off-white solid; mp 155–162 °C.

^{1}H NMR (400 MHz, acetone-d_6): δ = 10.73 (s, 1 H, indolyl H), 7.70–7.73 (m, 1 H, ArH), 7.47–7.54 (m, 2 H, ArH), 7.42–7.46 (m, 1 H, ArH), 7.31 (s, 1 H, ArH), 6.94 (dd, *J* = 1.83, 1 H, ArH), 6.69–6.72 (m, 1 H, ArH).

^{13}C NMR (100 MHz, acetone-d_6): δ = 137.5, 135.5, 134.1, 128.0, 126.8, 125.8, 121.3, 120.1, 119.8, 113.4, 110.7, 99.1.

MS (EI, 70 eV): *m*/*z* = 233 [M$^+$].

2-(2-Thienyl)indole (5d)
Yield: 179 mg (90%); off-white solid; mp 168–171 °C.[33]

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