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A palladium-catalyzed Barluenga cross-coupling – Reductive cyclization sequence to substituted indoles

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ABSTRACT

A short and flexible synthesis of substituted indoles employing two palladium-catalyzed reactions, a Barluenga cross-coupling of *p*-tosylhydrazones with 2-nitroarylhalides followed by a palladium –catalyzed, carbon monoxide–mediated reductive cyclization has been developed. A one-pot, two-step methodology was further developed, eliminating isolation and purification of the cross-coupling product. This was accomplished by utilizing the initially added 0.025 equivalents of bis(-triphenylphosphine)palladium dichloride, thus serving a dual role in the cross-coupling and the reductive cyclization. It was found that addition of 1,3-bis(diphenylphosphino)propane and carbon monoxide after completion of the Barluenga reaction afforded, in most cases, significantly better overall yields.

1. Introduction

The indole scaffold remains an important synthetic target and improving the efficiency of its synthesis is important in medicinal, natural product, and pharmaceutical chemistry. Reductive cyclization of 2-nitrostyrene derivatives to give substituted indoles can be achieved using a variety of reducing agents [1,2]. The two most commonly used variations are a) Cadogan-Sundberg reductive cyclization using phosphorous compounds, mainly triethylphosphite and triphenylphosphine, and b) reductions using carbon monoxide in the presence of a transition metal catalyst. The latter variant has emerged as a powerful alternative to the Cadogan-Sundberg reaction. The palladium–catalyzed carbon monoxide–mediated reaction was pioneered in a number of papers by the groups of Watanabe [3], Cenini [4], and Söderberg [5]. Reactions under 1 atm of carbon monoxide [6] and the use of formate esters [7], molybdenum hexacarbonyl [8], and carbon dioxide [9] as carbon monoxide surrogates were introduced later.

We have previously reported a reductive cyclization of 1-(2-nitrophenyl)-1-phenyl-1-propene (**2**) to give 2-methyl-3-phenylindole (**3**) in excellent isolated yield (Scheme 1) [10]. The cyclization precursor **2** was prepared by a Kosugi-Migita-Stille coupling of 2-iodonitrobenzene and vinyl-organotin **1**.

Kosugi–Migita–Stille cross–couplings of vinyl–tin reagents are synthetically important, in particular with respect to the reactions' tolerance of a wide range of functional group on the tin-reagent and the respectable to excellent yields frequently observed. The robustness of the carbon–tin bond, allows for the manipulation of functional groups present on the reagent prior to the coupling reaction, and is an important feature. However, a significant drawback is the toxicity of the tin reagents and more so the tin containing by-products.

In order to examine a different approach to cyclization precursors, such as **2**, and to evaluate the feasibility of a one–pot two–step sequence to indoles, tosylhydrazones derived from ketones were evaluated as possible cross-couplings partners. This palladium–catalyzed cross–coupling of tosylhydrazones with aryl halides, triflates and nonaflates, the Barluenga cross-coupling, have a number of attractive features [11–24]. Tosylhydrazones are readily prepared by treatment of tosylhydrazine with aldehydes or ketones and the palladium–catalyzed cross–coupling does not require a stoichiometric amount of an organometallic transmetallation reagent.

Barluenga coupling followed by a Cadogan-Sundberg reductive cyclization using triethylphosphite or triphenyl phosphine to give indoles and carbazoles [25–27] has been described by Hamze and Alami et al. (Scheme 2). The reported yields for their two–step, one–pot procedure were in many cases very good [25]. For

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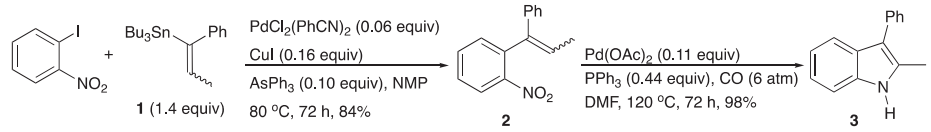
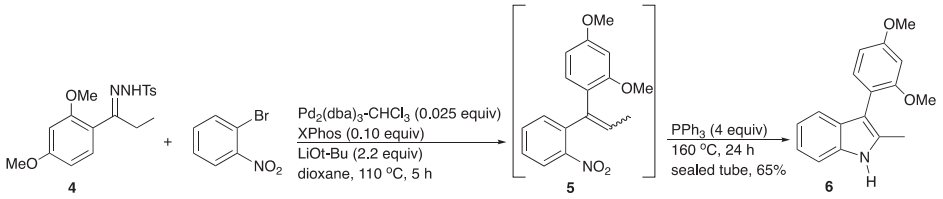


Scheme 1. Kosugi-Migita-Stille cross coupling – reductive cyclization sequence.



Scheme 2. Barluenga cross-coupling – reductive cyclization sequence.

example, Barluenga coupling of hydrazone **4** with 2-bromonitrobenzene followed by *in situ* treatment with triphenylphosphine at 160 °C gave indole **6** in 82% overall yield (Scheme 2). We report herein a related two–pot, two–step sequence and a more efficient, higher yielding, one–pot, two-step sequence using a palladium–catalyzed, carbon monoxide–mediated cyclization in the second reductive cyclization step to access indoles and azaindoles.

Results and Discussion Nine previously reported (**4**, **7**–**10**, **12**–**15**) and one novel *p*-tosylhydrazone (**11**) were prepared in 71–97% isolated yield by treatment of a selection of aromatic and aliphatic ketones with *p*-tosylhydrazide in methanol at 60 °C (Table 1). A variety of 2-bromonitrobenzenes (**16**–**27**) and 3-bromo-2-nitropyridine (**28**) were selected as cross-coupling partners in order to probe both electronic and steric effects on the subsequent reductive cyclization (see Table 1). All Barluenga cross-coupling reactions were performed using an arylhalide (1 equiv) and a *p*-tosylhydrazone (1.5 equiv) in the presence of bis(diphenylphosphino)palladium dichloride ($PdCl_2(PPh_3)_2$, 0.025 equiv) and lithium *tert*-butoxide (LiO*t*-Bu, 3.75 equiv) in 1,4-dioxane at 100 °C. In all but one case, the expected 2-nitrostyrenes **2**, **5, 29**–**42** and **44**–**45**, the latter from the only *p*-tosylhydrazone derived from an aliphatic ketone, and the pyridine analog **46** were isolated in 40–98% isolated yield (Table 1). While 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl (Xphos) is commonly employed as a ligand in these coupling reactions, the conditions developed by Ojha and Prabhu [19] described above worked well in a majority of the cases examined. However, attempted coupling of **16** with hydrazone **11** failed to give the expected coupling product **43** under the latter reaction conditions. This compound was obtained using a different catalyst system consisting of bis(dibenzylideneacetone) palladium and triphenyl phosphine (entry 17).

The twenty 2-nitro-α-substituted-styrenes were examined as possible substrates for a palladium–catalyzed cyclization using carbon monoxide as the stochiometric reductant. Palladium diacetate and triphenylphosphine were employed in our previously reported reductive cyclization of **2** to give 2-methyl-3-phenylindole (**3**), (Scheme 1) [10]. This particular catalyst–ligand combination appears not be as robust as the combination of palladium(II) acetate with both 1,3-bis(diphenylphosphino)propane (dppp) and 1,10-phenanthroline (phen) as ligands. The latter combination was selected for the present study and treatment of **2**, under 6 atm of carbon monoxide at 120 °C for 72 h, gave indole **3** in 66% yield (Table 1, entry 1). Substrates with a variety of functional groups residing on the nitro-arene containing aromatic ring were examined next. The two 3-substituted styrenes, **29** and **30**, examined gave the expected indoles **47** and **48** (entries 2–3) albeit, the latter in a lower yield. Cyclization of the isomeric methoxy-substituted 2-nitrostyrenes **31**–**32** furnished the corresponding indoles **49**–**50** in good yields (entries 4–5). In contrast, a low yield was observed from the remaining regioisomer **33** together with a substantial amount of unreacted strating material (entry 6). The reason for the sluggish reaction for this particular substrate is unclear since related reductive cyclizations of 2-nitrostyrenes having a methoxy-group adjacent to the nitro group have been described using palladium catalysts and carbon monoxide [6,28–30], a catalytic amount of bis(dimethylformamide)molybdenumdioxide together with triphenylphosphine [31], or electrochemically [32].

No significant difference in yield of product was observed employing the 5-methoxy (**32**), the 5-hydroxy (**34**), and the 5-chloro (**35**) substituted substrates (entries 5, 7, 8). Both the 5-amino- and 5-nitro-substituted styrenes **36** and **38**, respectively, gave the same urea functionalized indole **54** albeit, in very low yields (entries 9 and 11). It is unclear at what point in the overall transformation the 5-nitro group was reduced but it seem plausible that a common amino-functionalized intermediate is formed followed by carbonylation and reaction with dimethylamine [33]. The latter compound may be formed by *in situ* thermal decomposition of DMF. In contrast to **36** having a free amino group, the corresponding acetamide **37** was smoothly converted to the corresponding indole **55** in excellent yield (entry 10). Finaly, cyclization of the second substrate bearing an electron–withdrawing group, ester **39**, also furnished a low yield of indole (entry 12).

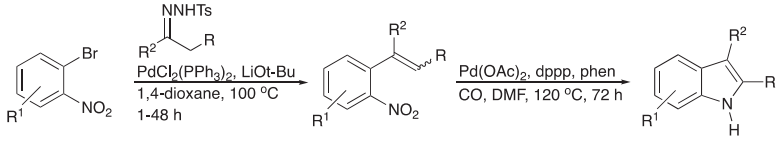
Reductive cyclization of nitrostyrenes derived from cross coupling of 2-bromo-1-nitrobenzene (**16**) with a variety of *p*-tosylhydrazones were examined next. Extending the carbon chain of the alkene did not interfere in the reaction and an excellent yield of 3-phenyl-2-propylindole (**57**) was realized from nitrostyrene **40** (entry 13). Nitrostyrenes **5** and **41**–**44**, prepared by the coupling of the hydrazones derived from 2,4-dimethoxypropiophenone (**4**), 4-methoxypropiophenone (**9**), α-tetralone (**10**), 5-methylindanone (**11**), and 3-acetylpyridine (**12**) all furnished the anticipated

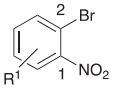
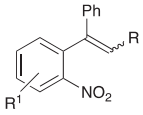
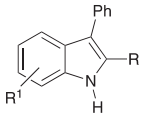
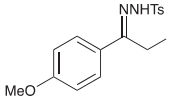
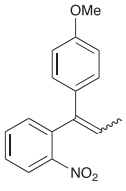
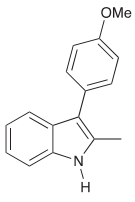
indoles **6** and **58**–**61** (entries 14–18). The sole example of a 2-nitro-α-substituted-styrene having an aliphatic α-substituent, compound **45**, also underwent reductive cyclization to give tetrahydrocarbazole **62** in very good yield (entry 19).

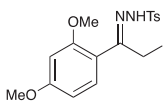
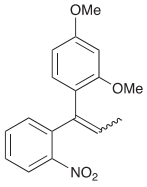
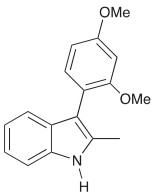
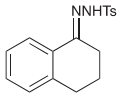
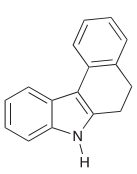
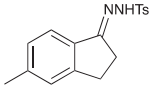
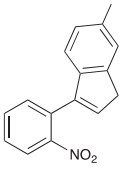
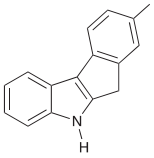
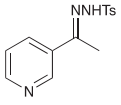
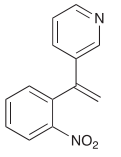
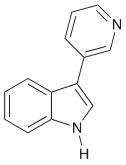
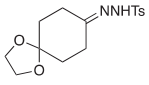
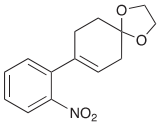
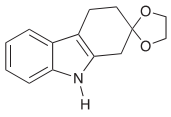
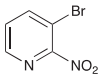
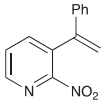
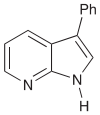
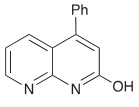
Finally, reductive cyclization of pyridine analog **46** gave in addition to the expected 3-phenyl-7-azaindole (**63**), 2-hydroxy-4-phenyl-1,8-naphthyridine (**64**) as a side product (entry 20). The latter product is the result of carbon monoxide insertion. Related CO-insertion – lactam formations have been observed in a few cases in palladium-catalyzed, carbon monoxide mediated reductive cyclizations [4,30]. The azaindole product was contaminated with a small amount of 2-amino-3-(1-phenyl-1-ethene-1-yl)pyridine (**65**), a product derived from reduction of the starting material **46**.

The feasibility of a one–pot, two–step sequence similar to the transformation of *p*-tosylhydrazone **4** to indole **6** seen in Scheme 2 was examined next and the results are summarized in Table 2. Barluenga cross–coupling of hydrazone **7** with 2-bromo-1-nitrobenzene **16** was executed as described above. After 2 h at 100 °C, $Pd(OAc)_2$, dppp and phen was added, the vessel was charged with CO (6 atm) and the resulting mixture was heated at 120 °C for an additional 72 h (entry 1). Standard workup and purification by chromatography gave indole **3** and nitrostyrene **2**, isolated in 73% and 29% yield, respectively. While complete conversion of **7** and **16** to **3** was not realized, the yield of indole was higher compared to the two–pot procedure seen in Table 1, entry 1 (59%). Charging the reaction vessel with CO after the first step without adding a catalyst

Table 1
Sequential Barluenga coupling – reductive cyclization



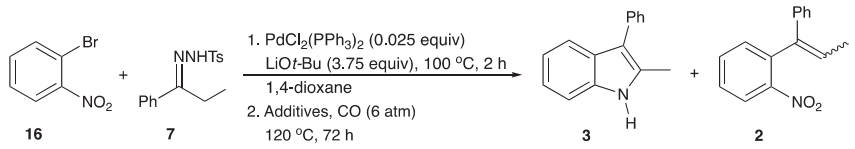
Entry[a]	Hydrazone[b]	2-Nitroarylbromide	2-Nitrostyrene[c]	Indole[d]
				
1	**7** (R = Me)	**16** (R^1 = H)	**2** (90%)	**3** (R^1 = H, 66%)
2		**17** (R^1 = 3-Me)	**29** (81%)	**47** (R^1 = 4-Me, 50%)
3		**18** (R^1 = 3-OMe)	**30** (98%)	**48** (R^1 = 4-OMe, 32%)
4		**19** (R^1 = 4-OMe)	**31** (82%)	**49** (R^1 = 5-OMe, 69%)
5		**20** (R^1 = 5-OMe)	**32** (95%)	**50** (R^1 = 6-OMe, 63%)
6		**21** (R^1 = 6-OMe)	**33** (91%)	**51** (R^1 = 7-OMe, 15%)[e,f]
7		**22** (R^1 = 5-OH)	**34** (65%)	**52** (R^1 = 6-OH, 60%)
8		**23** (R^1 = 5-Cl)	**35** (93%)	**53** (R^1 = 6-Cl, 68%)
9		**24** (R^1 = 5-NH_2)	**36** (67%)	**54** (R^1 = 6-$NHCONMe_2$, 13%)[g]
10		**25** (R^1 = 5-NHAc)	**37** (40%)	**55** (R^1 = 6-NHAc, 85%)
11		**26** (R^1 = 5-NO_2)	**38** (85%)	**54** (R^1 = 6-$NHCONMe_2$, 9%)[g]
12		**27** (R^1 = 5-CO_2Me)	**39** (57%)	**56** (R^1 = 6-CO_2Me, 35%)
13	**8** (R = Pr)	**16**	**40** (99%)	**57** (90%)
				
14	**9**	**16**	**41** (95%)	**58** (78%)

15		**4**		**5** (100%)	 **6** (59%)
16		**10**	**16**	**42** (90%)	 **59** (72%)
17		**11**	**16**	 **43** (78%)[h]	 **60** (44%)
18		**12**	**16**	 **44** (76%)	 **61** (98%)
19		**13**	**16**	 **45** (47%)	 **62** (81%)
20		 **14**	**28**	 **46** (89%)	 **63** (66%)[i]  **64** (18%)

a) For experimental details see the Experimental Section. b) Prepared from the corresponding ketone plus tosylhydrazine in methanol at 60 °C. c) $PdCl_2(PPh_3)_2$ (0.025 equiv) and LiO*t*-Bu (3.75 equiv) in 1,4-dioxane at 100 °C. d) $Pd(OAc)_2$ (0.10 equiv), dppp (~0.20 equiv), phen (~0.10 equiv) and CO (initial pCO = 6 atm) in DMF at 120 °C. e) Calculated from ~14:1 mixture of **51**/**33** from ^{1}H NMR. f) Starting material **33** was also recovered in 71%. g)R^1 = Me_2NCONH-. h) $Pd(dba)_2$ and PPh_3 was used. i) Isolated as a 20:1 mixture with 2-amino-3-(1-phenyl-1-ethene-1-yl)pyridine (**65**).

or ligands also produced **3** and **2** however, the yield of **3** was lower compared to entry 1 (entry 2). This result raised the possibility that the phosphine ligands (PPh_3 and/or dppp) were responsible for the reductive cyclization. However, nitrostyrene **2** was isolated in 79% yield as the sole product when carbon monoxide was excluded in the second step. No trace of indole **3** was observed by ^{1}H NMR of the crude reaction mixture (entry 3). The latter two entries indicated that a sufficient amount of palladium catalyst was still active after the initial coupling reaction and that carbon monoxide was crucial for the cyclization step. These observation opened the possibility of simply adding carbon monoxide and a ligand(s). Thus, both dppp and phen were added after 2 h resulting in similar yields, as observed in entry 1, of both indole **3** and styrene **2** (entry 4). Extending the reaction time to 120 h, in an attempt to obtain complete conversion of **2** to **3**, unfortunately resulted in pronounced lower yields of both products (entry 5). In a reaction wherein only phen was added (entry 6), similar yields were isolated as was observed in the absence of any added ligands or catalyst

Table 2
Optimization of a one-pot two-step sequence to 2-methyl-3-phenylindole.



Entry[a]		Pd(OAc)$_2$[b]	dppp[b]	phen[b]	3[c]	2[c]
1		+	+	+	73%	29%
2		−	−	−	31%	62%
3[d]	+		+	+	−	79%
4		−	+	+	66%	33%
5[e]		−	+	+	27%	10%
6		−	−	+	21%	73%
7		−	+	−	82%	18%
8[e]		−	+	−	86%	trace
9[f]		−	+	−	**98%**	**3%**

[a] See Experimental Section (entry 9) and Supporting Information (entries 1–9) for detailed descriptions.
[b] When applicable, 0.10 equiv of Pd(OAc)$_2$, 0.10 equiv of phen, and 0.20 equiv of dppp was used.
[c] The sum of the yields >100% is probably due to measuring errors and rounding of decimals.
[d] Reaction performed in the absence of CO.
[e] Reaction time for step 2, 120 h.
[f] Reaction temperature for step 2, 140 °C.

seen in entry 2. In contrast, addition of carbon monoxide and dppp after the first step produced a significantly higher yield of indole **3** (82%) in addition to 18% of styrene **2** (entry 7). The styrene was completely consumed upon extending the reaction time to 120 h but only a small insignificant increase in yield of **3** was realized (entry 8). Finally, all starting materials and the intermediately formed styrene **2** were almost quantitatively transformed into indole **3** by, rather than extending the reaction time, simply raising the reaction temperature to 140 °C (entry 9). Minor amounts of styrene was also observed. This one–pot, two–step procedure compared very favorably to the sequences depicted in Scheme 1 using a tin reagent and in Table 1 (entry 1) having an overall yield in two steps of 82% and 59%, respectively. It should be noted that the initially added 0.025 equivalents of palladium complex serves a dual role, a) as a catalyst for the Barluenga coupling and b) as a catalyst for the reductive cyclization.

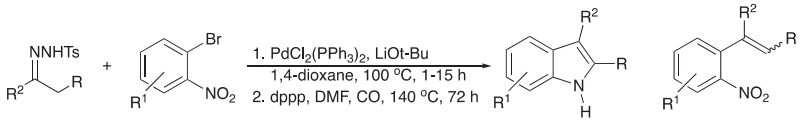
A selection of tosylhydrazones and 2-bromonitroaryls were examined as substrates for the one-pot, two-step sequence using the optimized reaction conditions seen in Table 2, entry 9. As can be seen in Table 3, higher isolated yields can be realized in most cases performing the two reactions in sequence in one pot without purification of the styrene intermediates. The largest improvement was observed employing 2-bromo-3-methoxy-1-nitrobenzene (**21**) and *p*-tosylhydrazone **7** affording indole **48** in quantitative yield; a more than three-fold increase compared to two-step one-pot procedure seen in Table 1 (Table 3, entry 8).

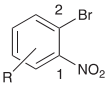
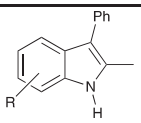
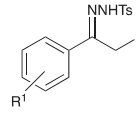
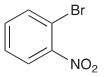
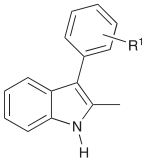
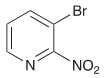
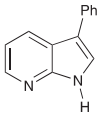
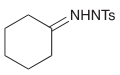
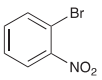
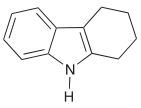
Isolated yields of indoles using *p*-tosylhydrazone **7** and either **17** or **22**–**23**, and from treatment of tosylhydrazone **14** with 3-bromo-2-nitropyridine (**28**) (entries 2, 8, and 10, and 15 in Table 3) were comparable to the corresponding two-step yields (entries 2, 7–8, and 20, Table 1). Treatment of hydrazone **14** with 3-bromo-2-nitropyridine (**28**) also furnished a minor amount of 2-amino-3-(1-phenyl-1-ethene-1-yl)pyridine (**65**) (entry 15). 1,8-Naphtyridine **64** was not observed in the one-pot procedure. While the one-pot procedure did furnish the expected indoles, a substantial amount of nitro-styrenes **29**, **34**–**35**, and **46** remained in the end of the reaction. Initial attempts to completely convert these intermediates to indoles by prolonging the reaction time, increasing the reaction temperature, or addition of more catalyst and/or ligands, failed to improve on the yield and the indole to nitrostyrene ratio. It was speculated that 1,4-dioxane may not be the optimum solvent for the reductive cyclization step. Thus, DMF was added as a co-solvent after complete consumption of the starting materials in the cross–coupling step. The addition of DMF resulted in significantly improved yields of indoles **47** and **52**–**53** (entries 3, 9, 11) Although no styrene intermediate remained after cross-coupling of **17** with **7** followed by reductive cyclization to give indole **47**, a lower but still significant amount of 2-nitrostyrene intermediates **34** and **35** were isolated in the two other cases. Attempts to further reduce or eliminate these by products by raising the reaction temperature to 150 °C in the reductive cyclization step, did not improve the isolated yields or the indole to styrene ratio (not shown in Table 3). In contrast, no improvement in yield or the indole to styrene ratio was seen in the synthesis of azaindole **63** upon addition of DMF (entry 16).

Substrates that performed poorly in the two-pot sequence remained problematic in the one-pot reaction. The one-pot procedure gave the same yield of 7-methoxyindole **51** and a somewhat higher yield of indole ester **56** (entries 7 and 13, respectively). Reaction of 2,4-dinitro-1-bromobenzene (**26**) with **7** did not go to completion however, the material that was consumed did not furnish any identifiable product (entry 12).

A comparison between the isolated yield of product reported by Hamze and Alami et al. and the present reaction sequence were made in three cases [25]. A significantly higher yield of 2-methyl-3-(2,4-dimethoxyphenyl)indole (**6**) was isolated (entry 14) while a similar yield of 3-phenyl-7-azaindole (**63**) and a slight improvement of 1,2,3,4-tetrahydrocarbazole (**66**) were obtained (entries 15 and 17) under the current reaction conditions.

Table 3
One-pot, two-step Barluenga coupling – reductive cyclization, a) See the Experimental Section for detailed descriptions. b) First %-yield is the isolated yield of pure product, the number in bracket and italics is the overall yield for two separate steps from Table 1 and the yield in bracket is the reported yield from reference 23. c) DMF was added to the reaction mixture after completion of the coupling reaction. d) Calculated from a ^{1}H NMR of an ~1:1.2 mixture of **51**/**21**. e) R^1 = Me_2NCONH- f) 2-Amino-3-(1-phenyl-1-ethene-1-yl)pyridine (**65**) was also isolated in 12% yield. g) Trace amounts of 2-amino-3-(1-phenyl-1-ethene-1-yl)pyridine (**65**) was also isolated.



Entry[a]	Hydrazone	2-Nitroarylbromide	Indole[b]		Coupling intermediate
					
1	**7**	**16** (R = H)	**3** (R^1 = H)	98% (*59%*)	**2** (3%)
2		**17** (R^1 = 3-Me)	**47** (R^1 = 4-Me)	52% (*41%*)	**29** (47%)
3		**17**	**47**	80%[c]	
4		**18** (R^1 = 3-OMe)	**48** (R^1 = 4-OMe)	100% (*31%*)	
5		**19** (R^1 = 4-OMe)	**49** (R^1 = 5-OMe)	92% (*57%*)	**31** (3%)
6		**20** (R^1 = 5-OMe)	**50** (R^1 = 6-OMe)	87% (*60%*)	
7		**21** (R^1 = 6-OMe)	**51** (R^1 = 7-OMe)	13%[d] (*15%*)	**33** (20%)[d]
8		**22** (R^1 = 5-OH)	**52** (R^1 = 6-OH)	39% (*39%*)	**34** (21%)
9		**22**	**52**	66%[c]	**34** (13%)
10		**23** (R^1 = 5-Cl)	**53** (R^1 = 6-Cl)	48% (*68%*)	**35** (47%)
11		**23**	**53**	67%[c]	**35** (24%)
12		**26** (R^1 = 5-NO_2)	**54** (R^1 = 6-NO_2)	– (*9%*)	**38** (36%)
13		**27** (R^1 = 5-CO_2Me)	**56** (R^1 = 6-CO_2Me)	31% (*20%*)	
					
14	**4** (R^1=2,4-diOMe)	**16**	**6** 82% (*59%*) {65%}[25]		**5** (7%)
					
15	**14**	**28**	**63** 60%[f] (*59%*) {55%}[25]		**46** (20%)
16	**14**	**28**	**63** 59%[c,g]		**46** (22%)
					
17	**15**	**16**	**66** 64% {54%}[25]		

a) See the Experimental Section for detailed descriptions. b) First %-yield is the isolated yield of pure product, the number in bracket and italics is the overall yield for two separate steps from Table 1 and the yield in bracket is the reported yield from reference 23. c) DMF was added to the reaction mixture after completion of the coupling reaction. d) Calculated from a ^{1}H NMR of an ~1:1.2 mixture of **51**/**21**. e) R^1 = Me_2NCONH- f) 2-Amino-3-(1-phenyl-1-ethene-1-yl)pyridine (**65**) was also isolated in 12% yield. g) Trace amounts of 2-amino-3-(1-phenyl-1-ethene-1-yl)pyridine (**65**) was also isolated.

2. Conclusions

A short and flexible two step sequence consisting of a Barluenga cross-coupling of aryl- and alkylketone-derived tosylhydrazones with 2-nitroarylhalides followed by a palladium-catalyzed, carbon monoxide-mediated reductive cyclization to give substituted indoles has been presented. The sequence was further developed into a one-pot, two-step transformation by addition of dppp and carbon monoxide after the initial Barluenga coupling reaction. Higher overall yields were realized in many cases using the latter process.

3. Experimental Section

3.1. General procedures

NMR spectra were determined in $CDCl_3$ at 400 MHz or 600 MHz (^{1}H NMR) and at 101 MHz or 151 MHz ($^{13}C\{^1H\}$ NMR) at ambient temperature. The chemical shifts are expressed in δ values relative to one of the following: tetramethylsilane (0.00 ppm, ^{1}H and $^{13}C\{^1H\}$), residual $CHCl_3$ (7.26 ppm, ^{1}H), $CDCl_3$ (77.0 ppm, $^{13}C\{^1H\}$), DMSO-d_6 (39.52 ppm, $^{13}C\{^1H\}$), and residual DMSO-d_6 (2.50 ppm,

^{1}H) internal standards. The multiplicity of each resonance observed in the ^{1}H NMR spectra are reported as, s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet. Hexanes and ethyl acetate (EtOAc) were distilled prior to use. 1,4-Dioxane and *N*,*N*-dimethylformamide (DMF) were purified/dried via two consecutive columns composed of activated alumina on a Glass Contours solvent purification system.

Chemicals prepared according to literature procedures (**4**, **7**–**10**, **12**–**15**, and **25**) have been footnoted the first time discussed in the Experimental Section. 2-Nitroaryl halides **16**–**24** and **26**–**28** and all other reagents were obtained from commercial sources and used as received. The reactions were performed in oven-dried glassware under a nitrogen or carbon monoxide atmosphere. All reactions were performed using an aluminum block having an appropriate size cavity for a reaction vessel and a separate drilled hole for a contact thermometer. The aluminum block was heated on a hot plate stirrer connected to the contact thermometer at a preset temperature.

Solvents were removed from reaction mixtures and products on a rotary evaporator at water aspirator pressure. Silica gel (SiO_2), 40–63 μm, 60 Å was used for column chromatography. Thin layer chromatography was performed on silica gel and the plates were visualized using UV-light. Reported melting points are uncorrected. Electrospray ionization HRMS data were obtained using an orbitrap mass analyzer.

5-Methyl-1-indanone 4-methylphenylsulfonylhydrazone (11). 5-Methyl-1-indanone (196 mg, 1.34 mmol) was added to a 60 °C solution of 4-methylbenzenesulphonylhydrazide (250 mg, 1.34 mmol) in methanol (40 mL). The mixture was stirred at 60 °C for 24 h. The reaction was allowed to cool to ambient temperature followed by removal of solvent under reduced pressure. The crude product was purified by chromatography (hexanes/EtOAc 1:1, R_f = 0.57) to give **11** (354 mg, 1.13 mmol, 84%) as a pale orange solid. mp = 217–218 °C; IR (ATR) 3211, 2920, 1598, 1395, 1346, 1327, 1167, 1067, 1004, 817, 763, 662 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.30 (d, *J* = 7.6 Hz, 2H), 7.17 (s, 1H), 7.09–7.04 (m, 2H), 3.05–3.00 (m, 2H), 2.64–2.59 (m, 2H), 2.41 (s, 3H), 2.35 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.4, 148.6, 144.0, 141.5, 135.5, 134.4, 129.5, 128.2, 128.1, 125.9, 121.9, 28.2, 26.7, 21.7, 21.6; HRMS (ESI) *m*/*z* [M+H]$^+$ calcd for $C_{17}H_{19}N_2O_2S$: 315.1162; found: 315.1162.

1-Nitro-2-(1-phenyl-1-propen-1-yl)benzene (2). [10] To a stirred solution of 2-bromonitrobenzene (**16**) (100 mg, 0.50 mmol), propiophenone 4-methylphenylsulfonylhydrazone (**7**) [34] (225 mg, 0.74 mmol) and $PdCl_2(PPh_3)_2$ (8.7 mg, 0.012 mmol) in 1,4-dioxane (10 mL) was added lithium *tert*-butoxide (147 mg, 1.84 mmol). Under a nitrogen atmosphere, the mixture was heated at 100 °C for 2 h. The reaction mixture was allowed to cool to ambient temperature. The mixture was diluted with water (40 mL) and extracted with EtOAc (3 × 40 mL). The combined organic phases were dried ($MgSO_4$), filtered and the solvents were removed under reduced pressure. The resulting crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.52) to give **2** (108 mg, 0.45 mmol, 90%, isomer ratio = 33:1) as a yellow solid.

mp = 64–65 °C; IR (ATR) 3027, 2915, 1526, 1492, 1442, 1361, 845, 759, 696 cm^{-1}; ^{1}H NMR of major isomer (400 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.64 (td, *J* = 7.6, 1.6 Hz, 1H), 7.51 (td, *J* = 7.2, 1.2 Hz, 1H), 7.33 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.28–7.15 (m, 5H), 6.27 (q, *J* = 6.8 Hz, 1H), 1.63 (d, *J* = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR of major isomer (101 MHz, $CDCl_3$) δ 149.4, 140.3, 138.4, 134.9, 132.9, 132.8, 128.3, 128.2, 127.1, 126.4, 125.1, 124.4, 15.5.

3-Methyl-1-nitro-2-(1-phenyl-1-propen-1-yl)benzene (29). Following the procedure described for **2**, 2-bromo-3-methylnitrobenzene (**17**) (150 mg, 0.69 mmol) was treated with hydrazone **7** (315 mg, 1.04 mmol) in the presence of $PdCl_2(PPh_3)_2$ (12 mg, 0.017 mmol) and lithium *tert*-butoxide (208 mg, 2.60 mmol) in 1,4-dioxane (10 mL) at 100 °C for 2 h. The crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.62) to give **29** (141 mg, 0.56 mmol, 81%, isomer ratio = 20:1) as a pale yellow solid. mp = 125–126 °C; IR (ATR) 3050, 2918, 2873, 1526, 1493, 1440, 803, 763, 752, 696 cm^{-1}; ^{1}H NMR of major isomer (400 MHz, $CDCl_3$) δ 7.76 (dd, *J* = 8.0, 0.4 Hz, 1H), 7.50 (dd, *J* = 7.8, 0.8 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 1H), 7.34–7.18 (m, 5H), 6.38 (q, *J* = 6.8 Hz, 1H), 2.16 (s, 3H), 1.54 (d, *J* = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR of major isomer (101 MHz, $CDCl_3$) δ 150.4, 139.6, 139.2, 136.5, 134.2, 133.2, 128.3, 127.9, 127.1, 125.8, 124.9, 121.5, 19.7, 15.2; HRMS (ESI) *m*/*z* [M+H]$^+$ calcd for $C_{16}H_{16}NO_2$: 254.1176; found: 254.1201.

3-Methoxy-1-nitro-2-(1-phenyl-1-propen-1-yl)benzene (30). Following the procedure described for **2**, 2-bromo-3-methoxynitrobenzene (**18**) (300 mg, 1.29 mmol) was treated with hydrazone **7** (587 mg, 1.94 mmol) in the presence of $PdCl_2(PPh_3)_2$ (23 mg, 0.033 mmol) and lithium *tert*-butoxide (388 mg, 4.85 mmol) in 1,4-dioxane (10 mL) at 100 °C for 7 h. The crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.50) to give **30** (339 mg, 1.26 mmol, 98%, isomer ratio = 33:1) as a yellow solid. mp = 89–90 °C; IR (ATR) 3015, 2975, 2940, 2843, 1602, 1526, 1438, 1367, 1264, 1052, 793, 758, 692 cm^{-1}; ^{1}H NMR of major isomer (400 MHz, $CDCl_3$) δ 7.53–7.43 (m, 2H), 7.27–7.16 (m, 6H), 6.33 (q, *J* = 6.8 Hz, 1H), 3.78 (s, 3H), 1.56 (d, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR of major isomer (101 MHz, $CDCl_3$) δ 157.8, 150.8, 140.1, 133.6, 129.0, 128.1, 126.9, 126.1, 125.9, 123.5, 115.8, 114.9, 56.5, 15.4; HRMS (ESI) *m*/*z* [M+H]$^+$ calcd for $C_{16}H_{16}NO_3$: 270.1125; found: 270.1139.

4-Methoxy-1-nitro-2-(1-phenyl-1-propen-1-yl)benzene (31). Following the procedure described for **2**, 2-bromo-4-methoxynitrobenzene (**19**) (100 mg, 0.43 mmol) was treated with hydrazone **7** (196 mg, 0.65 mmol) in the presence of $PdCl_2(PPh_3)_2$ (7.6 mg, 0.011 mmol) and lithium *tert*-butoxide (129 mg, 1.61 mmol) in 1,4-dioxane (10 mL) at 100 °C for 7 h. The crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.62) to give **31** (95 mg, 0.35 mmol, 82%, isomer ratio = 33:1) as a yellow solid. mp = 62–63 °C; IR (ATR) 3101, 3058, 2974, 2911, 1607, 1576, 1505, 1332, 1281, 1228, 1074, 1026, 833, 759, 699 cm^{-1}; ^{1}H NMR of major isomer (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 9.2 Hz, 1H), 7.28–7.17 (m, 5H), 6.96 (dd, *J* = 9.2, 2.8 Hz, 1H), 6.76 (d, *J* = 2.8 Hz, 1H), 6.24 (q, *J* = 6.8 Hz, 1H), 3.90 (s, 3H), 1.64 (d, *J* = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR of major isomer (101 MHz, $CDCl_3$) δ 163.1, 142.1, 140.1, 139.2, 137.9, 128.2, 127.3, 127.1126.2, 124.1, 117.4, 113.2, 55.9, 15.5; HRMS (ESI) *m*/*z* [M+H]$^+$ calcd for $C_{16}H_{16}NO_3$: 270.1125; found: 270.1122.

5-Methoxy-1-nitro-2-(1-phenyl-1-propen-1-yl)benzene (32). Following the procedure described for **2**, 2-bromo-5-methoxynitrobenzene (**20**) (200 mg, 0.86 mmol) was treated with hydrazone **7** (391 mg, 1.29 mmol) in the presence of $PdCl_2(PPh_3)_2$ (15 mg, 0.021 mmol) and lithium *tert*-butoxide (256 mg, 3.20 mmol) in 1,4-dioxane (10 mL) at 100 °C for 18 h. The crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.61) to give **32** (216 mg, 0.80 mmol, 95%, isomer ratio = 25:1) as an orange solid. mp = 65–66 °C; IR (ATR) 3078, 2977, 2914, 1615, 1522, 1496, 1355, 1295, 1258, 1234, 1067, 1034, 877, 796, 760, 698 cm^{-1}; ^{1}H NMR of major isomer (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 2.0 Hz, 1H), 7.27–7.15 (m, 7H), 6.25 (q, *J* = 6.4 Hz, 1H), 3.91 (s, 3H), 1.63 (d, *J* = 6.4 Hz, 3H); ^{13}C{^{1}H} NMR of major isomer (101 MHz, $CDCl_3$) δ 159.0, 149.7, 140.6, 138.2, 133.5, 128.1, 126.9, 126.8, 126.2, 125.0, 119.4, 109.0, 55.7, 15.4; HRMS (ESI) *m*/*z* [M+H]$^+$ calcd for $C_{16}H_{16}NO_3$: 270.1125; found: 270.1136.

6-Methoxy-1-nitro-2-(1-phenyl-1-propen-1-yl)benzene (33). Following the procedure described for **2**, 2-bromo-6-methoxynitrobenzene (**21**) (100 mg, 0.43 mmol) was treated with hydrazone **7** (196 mg, 0.65 mmol) in the presence of $PdCl_2(PPh_3)_2$

(7.6 mg, 0.011 mmol) and lithium *tert*-butoxide (129 mg, 1.61 mmol) in 1,4-dioxane (10 mL) at 100 °C for 7 h. The crude product was purified by chromatography (hexanes/EtOAc 8:2, $R_f = 0.31$) to give **33** (104 mg, 0.39 mmol, 91%, isomer ratio = 33:1) as a yellow solid. mp = 67–68 °C; IR (ATR) 3023, 2941, 2845, 1606, 1576, 1529, 1433, 1371, 1277, 1064, 852, 790, 756, 693 cm^{-1}; ^1H NMR of major isomer (400 MHz, $CDCl_3$) δ 7.45 (dd, J = 8.4, 7.8 Hz, 1H), 7.27–7.18 (m, 5H), 7.03 (dd, J = 8.0, 1.2 Hz, 1H), 6.82 (dd, J = 7.6, 1.2 Hz, 1H), 6.32 (q, J = 7.2 Hz, 1H), 3.93 (s, 3H), 1.66 (d, J = 7.2 Hz, 3H); ^{13}C NMR{^1H} of major isomer (101 MHz, $CDCl_3$) δ 150.8, 141.5, 140.0, 136.3, 133.9, 130.9, 128.2, 127.3, 127.2, 126.4, 122.7, 111.3, 56.3, 15.8; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{16}H_{16}NO_3$: 270.1125; found: 270.1128.

5-Hydroxy-1-nitro-2-(1-phenyl-1-propen-1-yl)benzene (34). Following the procedure described for **2**, 2-bromo-5-hydroxynitrobenzene (**22**) (100 mg, 0.46 mmol) was treated with hydrazone **7** (208 mg, 0.69 mmol) in the presence of $PdCl_2(PPh_3)_2$ (8.1 mg, 0.011 mmol), lithium *tert*-butoxide (139 mg, 1.74 mmol) in 1,4-dioxane (10 mL) at 100 °C for 8 h. The crude product was purified by chromatography (hexanes/EtOAc 8:2, $R_f = 0.67$) to give **34** (76 mg, 0.30 mmol, 65%, isomer ratio = 25:1) as a yellow solid. mp = 119–120 °C; IR (ATR) 3469, 3032, 2925, 2855, 1621, 1524, 1494, 1440, 1347, 1318, 1289, 1182, 870, 817, 752, 688, 614, 572, 522 cm^{-1}; ^1H NMR of major isomer (400 MHz, $CDCl_3$) δ 7.50 (d, J = 2.8 Hz, 1H), 7.28–7.11 (m, 7H), 6.25 (q, J = 6.8 Hz, 1H), 5.45 (br s, 1H), 1.63 (d, J = 6.8 Hz, 3H); $^{13}C\{^1H\}$ NMR of major isomer (101 MHz, $CDCl_3$) δ 155.3, 149.5, 140.6, 138.1, 133.9, 128.2, 127.1, 127.1, 126.3, 125.2, 120.52 111.4, 15.5; HRMS (ESI, negative mode) m/z $[M-H]^-$ calcd for $C_{15}H_{12}NO_3$: 254.0817; found: 254.0824.

5-Chloro-1-nitro-2-(1-phenyl-1-propen-1-yl)benzene (35). Following the procedure described for **2**, 2-bromo-5-chloronitrobenzene (**23**) (300 mg, 1.27 mmol) was treated with hydrazone **7** (461 mg, 1.95 mmol) in the presence of $PdCl_2(PPh_3)_2$ (22 mg, 0.031 mmol) and lithium *tert*-butoxide (381 mg, 4.76 mmol) in 1,4-dioxane (10 mL) at 100 °C for 4 h. The crude product was purified by chromatography (hexanes/EtOAc 9:1, $R_f = 0.88$) to give **35** (322 mg, 1.18 mmol, 93%, isomer ratio = 100:1) as a dark green solid. mp = 81–82 °C; IR (ATR) 3087, 3035, 2917, 2856, 1522, 1494, 1348, 1105, 904, 836, 753, 692 cm^{-1}; ^1H NMR of major isomer (600 MHz, $CDCl_3$) δ 8.02 (d, J = 1.8 Hz, 1H), 7.62 (dd, J = 7.8, 2.4 Hz, 1H), 7.30–7.20 (m, 5H), 7.16 (dd, J = 6.6, 1.8 Hz, 2H), 6.28 (q, J = 7.2 Hz, 1H), 1.63 (d, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR of major isomer (101 MHz, $CDCl_3$) δ 149.6, 139.9, 137.5, 134.0, 133.9, 133.4, 133.0, 128.3, 127.3, 126.3, 125.8, 124.7, 15.5; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{15}H_{13}ClNO_2$: 274.0629; found: 274.0656.

5-Amino-1-nitro-2-(1-phenyl-1-propen-1-yl)benzene (36). Following the procedure described for **2**, 5-amino-2-bromonitrobenzene (**24**) (200 mg, 0.92 mmol) was treated with hydrazone **7** (418 mg, 1.38 mmol) in the presence of $PdCl_2(PPh_3)_2$ (16 mg, 0.023 mmol) and lithium *tert*-butoxide (277 mg, 3.46 mmol) in 1,4-dioxane (10 mL) at 100 °C for 3 h. The crude product was purified by chromatography (hexanes/EtOAc 1:1, $R_f = 0.79$) to give **36** (157 mg, 0.62 mmol, 67%, isomer ratio = 20:1) as a dark brown solid. mp = 98–99 °C; IR (ATR) 3483, 3385, 3030, 2971, 2941, 2904, 2852, 1630, 1522, 1493, 1339, 1304, 817, 760, 699 cm^{-1}; ^1H NMR of major isomer (600 MHz, $CDCl_3$) δ 7.29 (d, J = 2.4 Hz, 1H), 7.26–7.19 (m, 5H), 7.06 (d, J = 7.8 Hz, 1H), 6.91 (dd, J = 8.4, 2.4 Hz, 1H), 6.21 (q, J = 7.2 Hz, 1H), 3.98 (br s, 2H), 1.64 (d, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR of major isomer (151 MHz, $CDCl_3$) δ 149.8, 146.5, 141.0, 138.5, 133.4, 128.1, 126.9, 126.3, 124.8, 124.0, 119.2, 109.8, 15.5; HRMS (ESI, negative mode) m/z $[M-H]^-$ calcd for $C_{15}H_{13}N_2O_2$: 253.0983; found: 253.0984.

5-(*N*-Acetylamino)-1-nitro-2-(1-phenyl-1-propen-1-yl)benzene (37). Following the procedure described for **2**, 5-(*N*-acetylamino)-2-bromonitrobenzene (**25**) [35] (219 mg, 0.85 mmol) was treated with hydrazone **7** (332 mg, 1.10 mmol) in the presence of $PdCl_2(PPh_3)_2$ (15 mg, 0.021 mmol) and lithium *tert*-butoxide (254 mg, 3.17 mmol) in 1,4-dioxane (10 mL) at 100 °C for 5.5 h. The crude product was purified by chromatography (hexanes/EtOAc 1:1, R_f = 0.24) to give **37** (102 mg (0.34 mmol, 40%, isomer ratio = 20:1) as a fluffy yellow solid. mp = 51–52 °C; IR (ATR) 3305, 3108, 3029, 2924, 2835, 1670, 1594, 1528, 1350, 1308, 1249, 822, 758, 694 cm^{-1}; ^1H NMR of major isomer (600 MHz, $CDCl_3$) δ 8.16 (d, J = 1.2 Hz, 1H), 7.87 (dd, J = 7.2, 1.8 Hz, 1H), 7.32 (br s, 1H), 7.22–7.18 (m, 3H), 7.21 (d, J = 7.8 Hz, 1H), 7.17 (dd, J = 8.4, 1.2 Hz, 2H), 6.26 (q, J = 7.2 Hz, 1H), 2.25 (s, 3H), 1.63 (d, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR of major isomer (151 MHz, $CDCl_3$) δ 169.6, 149.2, 140.4, 138.4, 138.1, 133.3, 130.1, 128.3, 127.2, 126.3, 125.3, 124.0, 115.4, 24.4, 15.5; HRMS (ESI, negative mode) m/z $[M-H]^-$ calcd for $C_{17}H_{15}N_2O_3$: 295.1088; found: 295.1089.

1,5-Dinitro-2-(1-phenyl-1-propen-1-yl)benzene (38). Following the procedure described for **2**, 2-bromo-1,5-dinitrobenzene (**26**) (200 mg, 0.81 mmol) was treated with hydrazone **7** (367 mg, 1.21 mmol) in the presence of $PdCl_2(PPh_3)_2$ (14 mg, 0.020 mmol) and lithium *tert*-butoxide (243 mg, 3.04 mmol) in 1,4-dioxane (10 mL) at 100 °C for 2.5 h. The crude product was purified by chromatography (hexanes/EtOAc 8:2, $R_f = 0.59$) to give **38** (197 mg, 0.69 mmol, 85%, isomer ratio = 33:1) as a pale yellow solid. mp = 117–118 °C; IR (ATR) 3108, 3083, 2965, 2915, 1596, 1516, 1441, 1352, 1123, 1065, 895, 834, 758, 737, 692 cm^{-1}; ^1H NMR of major isomer (400 MHz, $CDCl_3$) δ 8.86 (d, J = 2.4 Hz, 1H), 8.49 (dd, J = 8.8, 2.4 Hz, 1H), 7.57 (d, J = 8.8 Hz, 1H), 7.31–7.23 (m, 3H), 7.13 (dd, J = 7.4, 1.8 Hz, 2H), 6.35 (q, J = 7.2 Hz, 1H), 1.66 (d, J = 7.6 Hz, 3H); $^{13}C\{^1H\}$ NMR of major isomer (101 MHz, $CDCl_3$) δ 149.4, 147.1, 141.5, 139.2, 136.9, 134.3, 128.5, 127.8, 126.9, 126.8, 126.4, 120.1, 15.6; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{15}H_{13}N_2O_4$: 285.0870; found: 285.0872.

Methyl 3-nitro-4-(1-phenyl-1-propen-1-yl)benzoate (39). Following the procedure described for **2**, methyl 4-bromo-3-nitrobenzoate (**27**) (120 mg, 0.46 mmol) was treated with hydrazone **7** (209 mg, 0.69 mmol) in the presence of $PdCl_2(PPh_3)_2$ (8.1 mg, 0.011 mmol) and lithium *tert*-butoxide (138 mg, 1.72 mmol) in 1,4-dioxane (10 mL) at 100 °C for 1 h. The crude product was purified by chromatography (hexanes/EtOAc 8:2, $R_f = 0.65$) to give **39** (78 mg, 0.26 mmol, 57%, isomer ratio = 50:1) as a pale brown solid. mp = 81–82 °C; IR (ATR) 3043, 2954, 2873, 1726, 1531, 1350, 1284, 1242, 1112, 758, 697 cm^{-1}; ^1H NMR of major isomer (600 MHz, $CDCl_3$) δ 8.65 (d, J = 1.8 Hz, 1H), 8.29 (dd, J = 7.8, 1.8 Hz, 1H), 7.43 (d, J = 7.8 Hz, 1H), 7.28–7.21 (m, 3H), 7.16–7.14 (m, 2H), 6.30 (q, J = 7.2 Hz, 1H), 3.99 (s, 3H), 1.64 (d, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR of major isomer (151 MHz, $CDCl_3$) δ 164.9, 149.5, 139.8, 139.4, 137.8, 133.3, 133.2, 130.7, 128.4, 127.4, 126.4, 125.8, 125.6, 52.7, 15.5; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{16}NO_4$: 298.1074; found: 298.1077.

1-Nitro-2-(1-phenyl-1-penten-1-yl)benzene (40). Following the procedure described for **2**, 2-bromonitrobenzene (**16**) (200 mg, 0.99 mmol) was treated with valerophenone 4-methylphenylsulphonylhydrazone (**8**) [36] (491 mg, 1.49 mmol) in the presence of $PdCl_2(PPh_3)_2$ (17 mg, 0.024 mmol) and lithium *tert*-butoxide (297 mg, 3.71 mmol) in 1,4-dioxane (10 mL) at 100 °C for 2 h. The crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.67) to give **40** (262 mg, 0.98 mmol, 99%, isomer ratio = 33:1) as a yellow solid. mp = 55–56 °C; IR (ATR) 3031, 2955, 2927, 2866, 1606, 1519, 1351, 902, 847, 784, 760, 741, 729, 692 cm^{-1}; ^1H NMR of major isomer (400 MHz, $CDCl_3$) δ 8.02 (dd, J = 8.4, 1.2 Hz, 1H), 7.64 (td, J = 7.6, 1.6 Hz, 1H), 7.50 (td, J = 7.6, 1.6 Hz, 1H), 7.33 (dd, J = 8.0, 1.6 Hz, 1H), 7.28–7.17 (m, 5H), 6.18 (t, J = 7.6 Hz, 1H), 1.91 (q, J = 7.6 Hz, 2H), 1.42 (sextet, J = 7.6 Hz, 2H), 0.87 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR of major isomer (101 MHz, $CDCl_3$) δ 149.2, 140.4, 137.6, 135.2, 132.9, 132.8, 130.8, 128.3, 128.3,

127.2, 126.5, 124.5, 32.0, 22.6, 13.8; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{17}H_{18}NO_2$: 268.1332; found: 268.1334.

1-Nitro-2-[1-(4-methoxyphenyl)-1-propen-1-yl]benzene (41). Following the procedure described for **2**, 2-bromonitrobenzene (**16**) (200 mg, 0.99 mmol) was treated with 4-methoxypropiophenone 4-methylphenylsulfonylhydrazone (**9**) [37] (494 mg, 1.47 mmol) in the presence of $PdCl_2(PPh_3)_2$ (17 mg, 0.024 mmol) and lithium *tert*-butoxide (297 mg, 3.71 mmol) in 1,4-dioxane (10 mL) at 100 °C for 8 h. The crude product was purified by chromatography (hexanes/EtOAc 8:2, $R_f = 0.65$) to give **41** (253 mg, 0.94 mmol, 95%, isomer ratio = 50:1) as a yellow oil. IR (ATR) 3043, 2912, 2837, 1607, 1523, 1509, 1347, 1288, 1244, 1180, 1032, 821, 786, 758, 710 cm^{-1}; ^1H NMR of major isomer (400 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.63 (td, *J* = 7.6, 1.2 Hz, 1H), 7.49 (ddd, *J* = 8.4, 1.6 Hz, 1H), 7.32 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.10 (d, *J* = 9.2 Hz, 2H), 6.79 (d, *J* = 9.2 Hz, 2H), 6.16 (q, *J* = 6.8 Hz, 1H), 3.77 (s, 3H), 1.60 (d, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR of major isomer (101 MHz, $CDCl_3$) δ 158.8, 149.5, 137.8, 135.2, 133.2, 132.8, 132.7, 128.2, 127.5, 124.4, 123.4, 113.7, 55.2, 15.4; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{16}H_{16}NO_3$: 270.1125; found: 270.1129.

1-Nitro-2-[1-(2,4-dimethoxyphenyl)-1-propen-1-yl]benzene (5). Following the procedure described for **2**, 2-bromonitrobenzene (**16**) (120 mg, 0.59 mmol) was treated with 2,4-dimethoxypropiophenone 4-methylphenylsulfonylhydrazone (**4**) [24] (323 mg, 0.89 mmol) in the presence of $PdCl_2(PPh_3)_2$ (10.4 mg, 0.015 mmol), lithium *tert*-butoxide (178 mg, 2.22 mmol) in 1,4-dioxane (10 mL) at 100 °C for 8 h. The crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.50) to give **5** (177 mg, 0.59 mmol, 100%, isomer ratio = 25:1) as a yellow solid. mp = 65–66 °C; IR (ATR) 3012, 2964, 2936, 2842, 1605, 1526, 1500, 1456, 1436, 1355, 1304, 1208, 1156, 1132, 1048, 1032, 830, 787, 761, 703, 589 cm^{-1}; ^1H NMR of major isomer (400 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.53 (td, *J* = 7.6, 1.3 Hz, 1H), 7.41–7.34 (m, 2H), 7.11 (d, *J* = 8.4 Hz, 1H), 6.42 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.34 (d, *J* = 2.4 Hz, 1H), 6.11 (q, *J* = 6.4 Hz, 1H), 3.77 (s, 3H), 3.55 (s, 3H), 1.67 (d, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR of major isomer (101 MHz, $CDCl_3$) δ 160.2, 157.8, 149.2, 135.9, 135.2, 132.8, 131.9, 131.2, 128.3127.3, 123.8, 123.5, 104.2, 98.8, 55.2, 55.2, 15.5; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{17}H_{18}NO_3$: 300.1230; found: 300.1223.

1,2-Dihydro-4-(2-nitrophenyl)naphthalene (42). [22] Following the procedure described for **2**, 2-bromonitrobenzene (**16**) (200 mg, 0.99 mmol) was treated with α-tetralone 4-methylphenylsulfonylhydrazone (**10**) [24] (467 mg, 1.49 mmol) in the presence of $PdCl_2(PPh_3)_2$ (17 mg, 0.024 mmol) and lithium *tert*-butoxide (297 mg, 3.71 mmol) in 1,4-dioxane (10 mL) at 100 °C for 1.5 h. The crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.59) to give **42** (224 mg, 0.89 mmol, 90%) as a yellow solid. mp = 88–89 °C; IR (ATR) 3099, 3073, 3023, 2931, 2906, 2833, 1604, 1569, 1515, 1439, 1346, 1041, 848, 753, 738, 710, 704 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$ at 50 °C) δ 7.95 (d, *J* = 7.6 Hz, 1H), 7.60 (td, *J* = 7.2, 1.2 Hz, 1H), 7.47 (td, *J* = 7.6, 0.8 Hz, 1H), 7.40 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.19–7.09 (m, 2H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.58 (d, *J* = 8.0 Hz, 1H), 5.99 (t, *J* = 4.4 Hz, 1H), 2.90 (s, 2H), 2.45–2.40 (m, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 149.1, 136.6, 135.8, 135.6, 134.2, 132.8, 132.3, 128.2, 127.9, 127.6, 127.3, 126.4, 124.1, 123.6, 27.7, 23.3.

6-Methyl-1-(2-nitrophenyl)indene (43). Following the procedure described for **2**, 2-bromonitrobenzene (**16**) (100 mg, 0.50 mmol) was treated with hydrazone **11** (233 mg, 0.74 mmol) in the presence of $Pd(dba)_2$ (5.7 mg 0.010 mmol), PPh_3 (5.2 mg, 0.02 mmol) and lithium *tert*-butoxide (119 mg, 1.49 mmol) in 1,4-dioxane (10 mL) at 100 °C for 1 h. The resulting crude product was purified by chromatography (hexanes/EtOAc 8:2, $R_f = 0.67$) to give **43** (98 mg, 0.39 mmol, 78%) as a yellow-orange solid.

mp = 95–96 °C; IR (ATR) 3062, 2921, 2887, 1615, 1568, 1518, 1472, 1353, 1301, 1259, 1036, 851, 821, 786, 764, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.65 (td, *J* = 7.6, 1.2 Hz, 1H), 7.54–7.50 (m, 2H), 7.35 (s, 1H), 7.06 (d, *J* = 7.6 Hz, 1H), 6.95 (d, *J* = 7.6 Hz, 1H), 6.48 (t, *J* = 2.0 Hz, 1H), 3.52 (d, *J* = 2.0 Hz, 2H), 2.40 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 149.2, 143.8, 141.3, 141.0, 135.0, 132.7, 131.8, 131.3, 131.1, 128.5, 127.1, 125.0, 124.2, 118.9, 38.4, 21.4; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{16}H_{14}NO_2$: 252.1019; found: 252.1017.

1-Nitro-2-[1-(3-pyridinyl)-1-ethene-1-yl]benzene (44). Following the procedure described for **2**, 2-bromonitrobenzene (**16**) (200 mg, 0.99 mmol) was treated with 3-acetylpyridine 4-methylphenylsulfonylhydrazone (**12**) [24] (430 mg, 1.49 mmol) in the presence of $PdCl_2(PPh_3)_2$ (17 mg, 0.024 mmol) and lithium *tert*-butoxide (297 mg, 3.71 mmol) in 1,4-dioxane (10 mL) at 100 °C for 1.5 h. The crude product was purified by chromatography (hexanes/EtOAc 1:1, $R_f = 0.28$) to give **44** (170 mg, 0.75 mmol, 76%) as a pale brown solid. mp = 49–50 °C; IR (ATR) 3031, 2974, 1606, 1520, 1475, 1344, 1022, 912, 861, 816, 786, 764, 743, 710, 666 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.53–8.50 (m, 2H), 8.00 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.67 (td, *J* = 7.6, 1.2 Hz, 1H), 7.58–7.52 (m, 2H), 7.45 (dd, *J* = 7.2, 1.6 Hz, 1H), 7.23 (ddd, *J* = 8.0, 3.2, 0.8 Hz, 1H), 5.80 (s, 1H), 5.40 (s, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 149.1, 148.5, 147.7, 143.7, 135.7, 134.8, 133.6, 133.2, 132.3, 129.1, 124.6, 123.1, 117.0; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{13}H_{11}N_2O_2$: 227.0815; found: 227.0818.

8-(2-Nitrophenyl)-1,4-dioxaspiro[4.5]dec-7-ene (45). [38] Following the procedure described for **2**, 2-bromonitrobenzene (**16**) (150 mg, 0.74 mmol) was treated with 1,4-cyclohexanedione monoethylene ketal 4-methylphenylsulfonylhydrazone (**13**) [39] (482 mg, 1.49 mmol) in the presence of $PdCl_2(PPh_3)_2$ (52 mg, 0.074 mmol) and lithium *tert*-butoxide (238 mg, 2.97 mmol) in 1,4-dioxane (20 mL) at 100 °C for 48 h. The crude product was purified by chromatography (hexanes/EtOAc 7:3, R_f = 0.45) to give **45** (91 mg, 0.35 mmol, 47%) as a yellow solid. mp = 57–58 °C; IR (ATR) 2906, 2883, 1522, 1435, 1344, 1114, 1059, 1024, 866, 786, 744, 728, 693 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.53 (td, *J* = 7.2, 1.2 Hz, 1H), 7.39 (td, *J* = 8.0, 1.2 Hz, 1H), 7.33 (dd, *J* = 7.6, 1.2 Hz, 1H), 5.55–5.52 (m, 1H), 4.06–3.99 (m, 4H), 2.50–2.40 (m, 4H), 1.93 (t, *J* = 6.4 Hz, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 148.3, 138.5, 135.6, 132.6, 130.9, 127.7, 124.1, 123.7, 107.3, 64.5, 64.5, 36.0, 31.3, 28.8.

2-Nitro-3-(1-phenyl-1-ethene-1-yl)pyridine (46). [40] Following the procedure described for **2**, 3-bromo-1-nitropyridine (**28**) (100 mg, 0.493 mmol) was treated with hydrazone **14** (213 mg, 0.74 mmol) in the presence of $PdCl_2(PPh_3)_2$ (8.7 mg, 0.012 mmol) and LiO*t*-Bu (148 mg, 1.85 mmol) in 1,4-dioxane (10 mL) at 100 °C for 1 h. The crude product was purified by chromatography (hexanes/EtOAc 9:1 then 8:2, $R_f = 0.37$) to give **46** (99.7 mg, 0.441 mmol, 89%) as an orange oil. IR (ATR) 3058, 1538, 1367, 912, 866, 815, 705, 663 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.54 (dd, *J* = 4.7, 1.8 Hz, 1H), 7.87 (dd, *J* = 7.8, 1.9 Hz, 1H), 7.61 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.34–7.30 (m, 3H), 7.26–7.23 (m, 2H), 5.80 (s, 1H), 5.36 (s, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 157.5, 147.8, 143.5, 141.8, 138.2, 130.9, 128.6, 128.6, 127.3, 126.8, 117.4.

Optimization reactions of the one − pot, two − step procedure seen in Table 2.

Entry 1. To a threaded glass pressure tube was added 2-bromonitrobenzene (16) (100 mg, 0.50 mmol), hydrazone 7 (225 mg, 0.74 mmol) and $PdCl_2(PPh_3)_2$ (8.7 mg, 0.012 mmol), lithium *tert*-butoxide (149 g, 1.86 mmol) and 1,4-dioxane (8 mL). The pressure tube was equipped with pressure head and under a nitrogen atmosphere, the mixture was heated at 100 °C for 2 h. The vessel was cooled to ambient temperature and $Pd(OAc)_2$ (11.1 mg, 0.05 mmol), dppp (41 mg, 0.10 mmol) and phen (8.9 mg, 0.05 mmol) were added. The mixture was saturated with four cycles to 6 atm of carbon monoxide and heated at 120 °C for 72 h. The

resulting mixture was allowed to cool to ambient temperature. The mixture was diluted with water (30 mL) and extracted with EtOAc (3 × 30 mL). The combined organic phases were dried ($MgSO_4$), filtered and the solvents were removed under reduced pressure. The resulting crude product was purified by chromatography (hexanes/EtOAc 8:2, $R_f = 0.67$ and 0.51) to give in order of elution, 2 (34.6 mg, 0.145 mmol, 29%) as a yellow-orange solid and 3 (75.4 mg, 0.364 mmol, 73%) as a yellow gum.

Entry 2. Following the procedure above, 2-bromonitrobenzene (16) (100 mg, 0.50 mmol) was treated with hydrazone 7 (225 mg, 0.74 mmol) and $PdCl_2(PPh_3)_2$ (8.7 mg, 0.012 mmol), lithium *tert*-butoxide (149 g, 1.86 mmol) and 1,4-dioxane (8 mL) at 100 °C for 2 h, followed by addition of CO (pCO = 6 atm, 120 °C, 72 h). The crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.67 and 0.51) to give in order of elution, 2 (73.6 mg, 0.308 mmol, 62%) as a yellow-orange solid and 3 (32.0 mg, 0.154 mmol, 31%) as a yellow gum.

Entry 3. Following procedure above, 2-bromonitrobenzene (16) (100 mg, 0.50 mmol) was treated with hydrazone 7 (225 mg, 0.74 mmol) and $PdCl_2(PPh_3)_2$ (8.7 mg, 0.012 mmol), lithium *tert*-butoxide (149 g, 1.86 mmol) and 1,4-dioxane (8 mL) at 100 °C for 2 h, followed by addition of $Pd(OAc)_2$ (11.1 mg, 0.05 mmol), dppp (41 mg, 0.10 mmol) and phen (8.9 mg, 0.05 mmol) (120 °C, 72 h). The crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.67) to give in order of elution, 2 (94.0 mg, 0.393 mmol, 79%) as a yellow-orange solid.

Entry 4 Following the procedure above, 2-bromonitrobenzene (16) (100 mg, 0.50 mmol) was treated with hydrazone 7 (225 mg, 0.74 mmol) and $PdCl_2(PPh_3)_2$ (8.7 mg, 0.012 mmol), lithium *tert*-butoxide (149 g, 1.86 mmol) and 1,4-dioxane (8 mL) at 100 °C for 2 h, followed by addition of dppp (41 mg, 0.10 mmol), phen (8.9 mg, 0.05 mmol) and CO (pCO = 6 atm, 120 °C, 72 h). The crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.67 and 0.51) to give in order of elution, 2 (39.9 mg, 0.167 mmol, 33%) as a yellow-orange solid and 3 (68.8 mg, 0.332 mmol, 66%) as a yellow gum.

Entry 5. Following the procedure above, 2-bromonitrobenzene (16) (100 mg, 0.50 mmol) was treated with hydrazone 7 (225 mg, 0.74 mmol) and $PdCl_2(PPh_3)_2$ (8.7 mg, 0.012 mmol), lithium *tert*-butoxide (149 g, 1.86 mmol) and 1,4-dioxane (8 mL) at 100 °C for 2 h, followed by addition of dppp (41 mg, 0.10 mmol), phen (8.9 mg, 0.05 mmol) and CO (pCO = 6 atm, 120 °C, 120 h). The crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.67 and 0.51) to give in order of elution, 2 (11.6 mg, 0.048 mmol, 10%) as a yellow-orange solid and 3 (28.0 mg, 0.135 mmol, 27%) as a yellow gum.

Entry 6. Following the procedure above, 2-bromonitrobenzene (16) (100 mg, 0.50 mmol) was treated with hydrazone 7 (225 mg, 0.74 mmol) and $PdCl_2(PPh_3)_2$ (8.7 mg, 0.012 mmol), lithium *tert*-butoxide (149 g, 1.86 mmol) and 1,4-dioxane (8 mL) at 100 °C for 2 h, followed by addition of phen (8.9 mg, 0.05 mmol) and CO (pCO = 6 atm, 120 °C, 72 h). The crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.67 and 0.51) to give in order of elution, 2 (87.6 mg, 0.366 mmol, 73%) as a yellow-orange solid and 3 (21.6 mg, 0.104 mmol, 21%) as a yellow gum.

Entry 7. Following the procedure above, 2-bromonitrobenzene (16) (100 mg, 0.50 mmol) was treated with hydrazone 7 (225 mg, 0.74 mmol) and $PdCl_2(PPh_3)_2$ (8.7 mg, 0.012 mmol), lithium *tert*-butoxide (149 g, 1.86 mmol) and 1,4-dioxane (8 mL) at 100 °C for 2 h, followed by addition of dppp (41 mg, 0.10 mmol) and CO (pCO = 6 atm, 120 °C, 72 h). The crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.67 and 0.51) to give in order of elution, 2 (21.5 mg, 0.090 mmol, 18%) as a yellow-orange solid and 3 (84.5 mg, 0.408 mmol, 82%) as a yellow gum.

Entry 8. Following the procedure above, 2-bromonitrobenzene (16) (100 mg, 0.50 mmol) was treated with hydrazone 7 (225 mg, 0.74 mmol) and $PdCl_2(PPh_3)_2$ (8.7 mg, 0.012 mmol), lithium *tert*-butoxide (149 g, 1.86 mmol) and 1,4-dioxane (8 mL) at 100 °C for 2 h, followed by addition of dppp (41 mg, 0.10 mmol) and CO (pCO = 6 atm, 120 °C, 120 h). The crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.51) to give 3 (88.8 mg, 0.428 mmol, 86%) as a yellow gum.

Entry 9. Following the procedure above, 2-bromonitrobenzene (16) (100 mg, 0.50 mmol) was treated with hydrazone 7 (225 mg, 0.74 mmol) and $PdCl_2(PPh_3)_2$ (8.7 mg, 0.012 mmol), lithium *tert*-butoxide (149 g, 1.86 mmol) and 1,4-dioxane (8 mL) at 100 °C for 2 h, followed by addition of dppp (41 mg, 0.10 mmol) and CO (pCO = 6 atm, 140 °C, 72 h). The crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.67 and 0.51) to give in order of elution, 2 (3.9 mg, 0.016 mmol, 3%) as a yellow-orange solid and 3 (101 mg, 0.49 mmol, 98%) as a yellow gum.

2-Methyl-3-phenyl-1*H*-indole (3) [10]. Procedure A: To a threaded glass pressure tube was added styrene 2 (73 mg, 0.31 mmol), palladium diacetate ($Pd(OAc)_2$, 6.8 mg, 0.03 mmol), 1,3-bis(diphenylphosphino)propane (dppp, 25 mg, 0.06 mmol), 1,10-phenanthroline (phen, 5.5 mg, 0.03 mmol) and DMF (3 mL). After fitting a pressure head to the tube, the mixture was saturated with four cycles to 6 atm of carbon monoxide and heated at 120 °C for 72 h. The resulting mixture was allowed to cool to ambient temperature. The mixture was diluted with water (30 mL) and extracted with EtOAc (3 × 30 mL). The combined organic phases were dried ($MgSO_4$), filtered and the solvents were removed under reduced pressure. The resulting crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.51) to give 3 (43 mg, 0.21 mmol, 66%) as a yellow gum. IR (ATR) 3399, 3053, 2918, 1602, 1496, 1458, 1427, 1305, 1254, 1186, 1075, 980, 769, 740, 700, 659 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (br s, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.52 (dd, J = 8.0, 1.2 Hz, 2H), 7.46 (td, J = 7.6, 2.0 Hz, 2H), 7.35–7.27 (m, 2H), 7.17 (td, J = 7.2, 1.2 Hz, 1H), 7.11 (td, J = 7.6, 0.4 Hz, 1H), 2.50 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 135.4, 135.2, 131.4, 129.4, 128.4, 127.8, 125.7, 121.5, 119.9, 118.7, 114.4, 110.3, 12.4.

Procedure B: To a threaded glass pressure tube was added 2-bromonitrobenzene (16) (100 mg, 0.50 mmol), hydrazone 7 (225 mg, 0.74 mmol) and $PdCl_2(PPh_3)_2$ (8.7 mg, 0.012 mmol), lithium *tert*-butoxide (149 g, 1.86 mmol) and 1,4-dioxane (8 mL). The pressure tube was equipped with pressure head and under a nitrogen atmosphere, the mixture was heated at 100 °C for 2 h. The vessel was cooled to ambient temperature and dppp (41 mg, 0.10 mmol) was added. The mixture was saturated with four cycles to 6 atm of carbon monoxide and heated at 140 °C for 72 h. The resulting mixture was allowed to cool to ambient temperature. The mixture was diluted with water (30 mL) and extracted with EtOAc (3 × 30 mL). The combined organic phases were dried ($MgSO_4$), filtered and the solvents were removed under reduced pressure. The resulting crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.51) to give 3 (101 mg, 0.49 mmol, 98%) as a yellow gum.

2,4-Dimethyl-3-phenyl-1*H*-indole (47). Following Procedure A, styrene 29 (80 mg, 0.32 mmol) was treated with CO (pCO = 6 atm) in the presence of $Pd(OAc)_2$ (7.1 mg, 0.032 mmol), dppp (26 mg, 0.063 mmol) and phen (6 mg, 0.033 mmol) in DMF (3 mL) at 120 °C for 72 h. The crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.52) to give 47 (35 mg, 0.16 mmol, 50%) as an off-white solid.

Following Procedure B but with the addition of DMF. 2-Bromo-3-methylnitrobenzene (17) (100 mg, 0.46 mmol) was treated with hydrazone 7 (208 mg, 0.69 mmol), $PdCl_2(PPh_3)_2$ (8.1 mg, 0.011 mmol), lithium *tert*-butoxide (139 mg, 1.74 mmol) in 1,4-dioxane (8 mL) at 100 °C for 2 h, followed by addition of dppp

(38 mg, 0.092 mmol) and DMF (3 mL) under CO (pCO = 6 atm, 140 °C, 72 h). The crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.52) to give impure 47 which was repurified (hexanes/CH_2Cl_2, 8:2 follwed by 7:3) affording pure 47 (82 mg, 0.37 mmol, 80%) as an off-white solid.

2,4-Dimethyl-3-phenyl-1*H*-indole (47) and 3-Methyl-1-nitro-2-(1-phenyl-1-propen-1-yl)benzene (29). Following Procedure B, 2-bromo-3-methyl-1-nitrobenzene (22) (100 mg, 0.46 mmol) was treated with hydrazone 7 (210 mg, 0.69 mmol), $PdCl_2(PPh_3)_2$ (8.1 mg, 0.012 mmol), lithium *tert*-butoxide (139 mg, 1.74 mmol) in 1,4-dioxane (8 mL) at 100 °C for 2 h, followed by addition of dppp (38 mg, 0.092 mmol) under CO (pCO = 6 atm, 140 °C, 72 h). The crude product was purified by chromatography (hexanes/EtOAc 8:2) to give, in order of elution, 29 (55 mg, 0.217 mmol, 47%, R_f = 0.62) and 47 (53 mg, 0.24 mmol, 52%, R_f = 0.52) both as yellow solids.

Analytical data for 47: mp = 126–127 °C; IR (ATR) 3375, 3024, 2918, 1604, 1567, 1495, 1452, 1433, 1415, 1324, 1314, 1256, 1194, 1155, 1081, 984, 778, 748, 703, 671 cm^{-1}.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (br s, 1H), 7.41–7.30 (m, 5H), 7.19 (d, J = 8.4 Hz, 1H), 7.04 (t, J = 7.6 Hz, 1H), 6.81 (d, J = 7.2 Hz, 1H), 2.29 (s, 3H), 2.13 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 137.0, 135.0, 131.7, 131.5, 130.2, 127.5, 126.7, 126.3, 121.3, 121.2, 115.6, 108.1, 20.4, 11.9; HRMS (ESI, negative mode) m/z [M − H]$^-$ calcd for $C_{16}H_{14}N$: 220.1132; found: 220.1128.

4-Methoxy-2-methyl-3-phenyl-1*H*-indole (48). Following Procedure A, styrene 30 (75 mg, 0.28 mmol) was treated with CO (pCO = 6 atm) in the presence of $Pd(OAc)_2$ (6.2 mg, 0.028 mmol), dppp (23 mg, 0.056 mmol) and phen (5.0 mg, 0.028 mmol) in DMF (3 mL) under CO (pCO = 6 atm) at 120 °C for 72 h. The crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.50) to give 48 (22 mg, 0.09 mmol, 32%) as an orange gum.

Following Procedure B, 2-bromo-3-methoxynitrobenzene (18) (100 mg, 0.43 mmol) was treated with hydrazone 7 (196 mg, 0.65 mmol), $PdCl_2(PPh_3)_2$ (7.6 mg, 0.011 mmol), lithium *tert*-butoxide (129 mg, 1.61 mmol) in 1,4-dioxane (8 mL) at 100 °C for 7 h, followed by addition of dppp (36 mg, 0.087 mmol) under CO (pCO = 6 atm, 140 °C, 72 h). The crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.50) to give 48 (102 mg, 0.43 mmol, 100%) as an orange gum. IR (ATR) 3396, 3058, 2930, 2835, 1600, 1589, 1554, 1506, 1496, 1437, 1426, 1338, 1260, 1104, 1197, 980, 755, 732, 701, 667 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (br s, 1H), 7.44 (td, J = 7.6, 1.6 Hz, 2H), 7.37 (t, J = 7.6 Hz, 2H), 7.26 (tt, J = 6.8, 1.6 Hz, 1H), 7.06 (t, J = 8.0 Hz, 1H), 6.93 (d, J = 8.4 Hz, 1H), 6.51 (d, J = 8.0 Hz, 1H), 3.70 (s, 3H), 2.35 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 153.9, 136.7, 136.1, 131.1, 130.5, 127.1, 125.5, 122.0, 117.2, 114.3, 103.8, 100.7, 55.2, 12.2; HRMS (ESI, negative mode) m/z [M − H]$^-$ calcd for $C_{16}H_{14}NO$: 236.1081; found: 236.1076.

5-Methoxy-2-methyl-3-phenyl-1*H*-indole (49) [41]. Following Procedure A, styrene 31 (44 mg, 0.16 mmol) was treated with CO (pCO = 6 atm) in the presence of $Pd(OAc)_2$ (3.6 mg, 0.018 mmol), dppp (14 mg, 0.034 mmol) and phen (3 mg, 0.017 mmol) in DMF (3 mL) at 120 °C for 72 h. The crude product was purified by chromatography (hexanes/EtOAc 7:3, R_f = 0.67) to give 49 (27 mg, 0.11 mmol, 69%) as a red solid.

Following Procedure B, 2-bromo-4-methoxynitrobenzene (19) (100 mg, 0.43 mmol) was treated with hydrazone 7 (196 mg, 0.65 mmol), $PdCl_2(PPh_3)_2$ (7.6 mg, 0.011 mmol), lithium *tert*-butoxide (129 mg, 1.61 mmol) in 1,4-dioxane (8 mL) at 100 °C for 7 h, followed by addition of dppp (36 mg, 0.087 mmol) under CO (pCO = 6 atm, 140 °C, 72 h). The crude product was purified by chromatography (hexanes/EtOAc 7:3, R_f = 0.67) to give 49 (94 mg, 0.40 mmol, 92%) as a red solid. mp = 69–70 °C; IR (ATR) 3402, 3381, 3000, 2950, 2827, 1619, 1600, 1481, 1439, 1269, 1221, 1148, 1026, 838, 799, 766, 702, 658 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (br s, 1H), 7.53–7.44 (m, 4H), 7.33–7.28 (m, 1H), 7.22 (d, J = 8.8 Hz, 1H), 7.13 (d, J = 2.4 Hz, 1H), 6.82 (dd, J = 8.8, 2.4 Hz, 1H), 3.81 (s, 3H), 2.49 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 154.5, 135.5, 132.3, 130.2, 129.3, 128.5, 128.2, 125.7, 114.3, 111.3, 111.0, 101.0, 55.9, 12.5.

6-Methoxy-2-methyl-3-phenyl-1*H*-indole (50) [42]. Following procedure A, styrene 32 (73 mg, 0.27 mmol) was treated with CO (pCO = 6 atm) in the presence of $Pd(OAc)_2$ (6.1 mg, 0.027 mmol), dppp (22 mg, 0.053 mmol) and phen (4.9 mg, 0.027 mmol) in DMF (3 mL) at 120 °C for 72 h. The crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.38) to give 50 (41.0 mg, 0.17 mmol, 63%) as a pale orange solid.

Following Procedure B, 2-bromo-5-methoxynitrobenzene (20) (100 mg, 0.43 mmol) was treated with hydrazone 7 (196 mg, 0.65 mmol), $PdCl_2(PPh_3)_2$ (7.6 mg, 0.011 mmol), lithium *tert*-butoxide (129 mg, 1.61 mmol) in 1,4-dioxane (8 mL) at 100 °C for 7 h, followed by addition of dppp (36 mg, 0.087 mmol) under CO (pCO = 6 atm, 140 °C, 72 h). The crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.38) to give 50 (89 mg, 0.38 mmol, 87%) as a pale orange solid. mp = 155–156 °C; IR (ATR) 3331, 2963, 2934, 1625, 1600, 1558, 1492, 1455, 1419, 1314, 1240, 1199, 1165, 1115, 947, 823, 808, 767, 746, 707, 661 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (br s, 1H), 7.56–7.41 (m, 5H), 7.29 (t, J = 7.2 Hz, 1H), 6.85 (d, J = 2.0 Hz, 1H), 6.78 (dd, J = 8.8, 2.0 Hz, 1H), 3.85 (s, 3H), 2.48 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 156.1, 135.9, 135.5, 130.0, 129.2, 128.5, 125.7, 122.2, 119.4, 114.2, 109.3, 94.4, 55.7, 12.4.

7-Methoxy-2-methyl-3-phenyl-1*H*-indole (51). Following Procedure A, styrene 33 (81.5 mg, 0.303 mmol) was treated with CO (pCO = 6 atm) in the presence of $Pd(OAc)_2$ (6.8 mg, 0.03 mmol), dppp (25 mg, 0.061 mmol) and phen (5.5 mg, 0.03 mmol) in DMF (3 mL) at 120 °C for 72 h. The crude product was purified by chromatography (hexanes/EtOAc, 4:1, R_f = 0.61) to give a mixture of 33 and 51 (~7:1 by ^{1}H NMR, 68.8 mg). The mixture was chromatographed (hexanes/CH_2Cl_2, 1:1) to give, in order of elution, 33 (56.7 mg, 0.214 mmol, 71%, R_f = 0.48) and a mixture of 51 and 33 (~14:1 by ^{1}H NMR, calculated from spectrum 10.6 mg of 51, 0.045 mmol, 15%, R_f = 0.38) both as a pale yellow solids.

Following Procedure B, 2-bromo-6-methoxynitrobenzene (21) (100 mg, 0.43 mmol) was treated with hydrazone 7 (196 mg, 0.65 mmol), $PdCl_2(PPh_3)_2$ (7.6 mg, 0.011 mmol), lithium *tert*-butoxide (129 mg, 1.61 mmol) in 1,4-dioxane (8 mL) at 100 °C for 7 h, followed by addition of dppp (36 mg, 0.087 mmol) under CO (pCO = 6 atm, 140 °C, 72 h). The crude product was purified by chromatography (hexanes/CH_2Cl_2 1:1, R_f = 0.38) to give a mixture of 51 and 33 (~1:1.2 by ^{1}H NMR, 42 mg, 51 calculated from ^{1}H NMR: 19 mg, 0.078 mmol, 13%). Analytical data from a 14:1 mixture of 51/33: mp = 89–91 °C; IR (ATR) 3431, 3413, 2930, 2850, 1579, 1495, 1438, 1418, 1390, 1370, 1264, 1246, 1095, 987, 763, 781, 732, 705 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.21 (br s, 1H), 7.51 (dd, J = 7.8, 1.2 Hz, 2H), 7.45 (t, J = 7.8 Hz, 2H), 7.31–7.27 (m, 2H), 7.03 (t, J = 7.2 Hz, 1H), 6.64 (d, J = 7.2 Hz, 1H), 3.97 (s, 3H), 2.51 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 145.6, 135.6, 129.4, 129.1, 128.4, 126.5, 125.7, 125.5, 120.3, 114.9, 111.7, 101.7, 55.4, 12.6; HRMS (ESI, negative mode) m/z [M − H]$^-$ calcd for $C_{16}H_{14}NO$: 236.1081; found: 236.1078.

6-Hydroxy-2-methyl-3-phenyl-1*H*-indole (52). Following Procedure A, styrene 34 (64 mg, 0.25 mmol) was treated with CO (pCO = 6 atm) in the presence of $Pd(OAc)_2$ (5.6 mg, 0.027 mmol), dppp (21 mg, 0.051 mmol) and phen (4.5 mg, 0.025 mmol) in DMF (3 mL) at 120 °C for 72 h. The crude product was purified by chromatography (hexanes/EtOAc 7:3, R_f = 0.16) to give 52 (33.0 mg, 0.15 mmol, 60%) as pale orange white solid.

6-Hydroxy-2-methyl-3-phenyl-1*H*-indole (52) and 5-Hydroxy-1-nitro-2-(1-phenyl-1-propen-1-yl)benzene (34). Following Procedure B, 2-bromo-5-hydroxynitrobenzene (22) (100 mg, 0.46 mmol) was treated with hydrazone 7 (208 mg, 0.69 mmol), $PdCl_2(PPh_3)_2$ (8.1 mg, 0.011 mmol), lithium *tert*-butoxide (139 mg,

1.74 mmol) in 1,4-dioxane (8 mL) at 100 °C for 8 h, followed by addition of dppp (38 mg, 0.092 mmol) under CO (pCO = 6 atm, 140 °C, 72 h). The crude product was purified by chromatography (hexanes/EtOAc 7:3) to give, in order of elution, 34 (25 mg, 0.098 mmol, 21%, R_f = 0.60) as a brown oil and 52 (40.0 mg, 0.179 mmol, 39%, R_f = 0.16) as a pale orange solid.

Following Procedure B but with the addition of DMF. 2-Bromo-5-hydroxynitrobenzene (22) (100 mg, 0.46 mmol) was treated with hydrazone 7 (208 mg, 0.69 mmol), $PdCl_2(PPh_3)_2$ (8.1 mg, 0.011 mmol), lithium *tert*-butoxide (139 mg, 1.74 mmol) in 1,4-dioxane (8 mL) at 100 °C for 8 h, followed by addition of dppp (38 mg, 0.092 mmol) and DMF (3 mL) under CO (pCO = 6 atm, 140 °C, 72 h). The crude product was purified by chromatography (hexanes/EtOAc 7:3) to give, in order of elution, 34 (15 mg, 0.059 mmol, 13%, R_f = 0.60) as a brown oil and 52 (68 mg, 0.305 mmol, 66%, R_f = 0.16) as a pale orange solid.

Analytical data for 52: mp = 134–135 °C; IR (ATR) 3391, 3263, 2921, 1732, 1629, 1602, 1629, 1493, 1455, 1324, 1232, 1151, 804, 763, 702, 659, 531, 519 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (br s, 1H), 7.52–7.42 (m, 5H), 7.29 (t, J = 6.8 Hz, 1H), 6.81 (d, J = 2.0 Hz, 1H), 6.66 (dd, J = 8.4, 2.4 Hz, 1H), 4.60 (br s, 1H), 2.48 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 151.4, 136.0, 135.4, 130.2, 129.2, 128.5, 125.7, 122.4, 119.4, 114.1, 109.5, 96.5, 12.4.

6-Chloro-2-methyl-3-phenyl-1*H*-indole (53). Following Procedure A, styrene 35 (160 mg, 0.59 mmol) was treated with CO (pCO = 6 atm) in the presence of $Pd(OAc)_2$ (13 mg, 0.053 mmol), dppp (48 mg, 0.012 mmol) and phen (11 mg, 0.061 mmol) in DMF (3 mL) at 120 °C for 72 h. The crude product was purified by chromatography (hexanes/EtOAc 9:1, R_f = 0.58) to give 53 (96 mg, 0.40 mmol, 68%) as a white solid.

6-Chloro-2-methyl-3-phenyl-1*H*-indole (53) and 5-Chloro-1-nitro-2-(1-phenyl-1-propen-1-yl)benzene (35). Following Procedure B, 2-bromo-5-chloronitrobenzene (23) (100 mg, 0.42 mmol) was treated with hydrazone 7 (192 mg, 0.64 mmol), $PdCl_2(PPh_3)_2$ (7.4 mg, 0.01 mmol), lithium *tert*-butoxide (127 mg, 1.59 mmol) in 1,4-dioxane (8 mL) at 100 °C for 4 h, followed by addition of dppp (38 mg, 0.092 mmol) under CO (pCO = 6 atm, 140 °C, 72 h). The crude product was purified by chromatography (hexanes/EtOAc 9:1) to give, in order of elution, 35 (54 mg, 0.197 mmol, 47%, R_f = 0.88) as a yellow-orange solid and 53 (49 mg, 0.20 mmol, 48%, R_f = 0.58) as a yellow solid.

Following Procedure B but with the addition of DMF. 2-Bromo-5-chloronitrobenzene (23) (100 mg, 0.42 mmol) was treated with hydrazone 7 (192 mg, 0.64 mmol), $PdCl_2(PPh_3)_2$ (7.4 mg, 0.01 mmol), lithium *tert*-butoxide (127 mg, 1.59 mmol) in 1,4-dioxane (8 mL) at 100 °C for 4 h, followed by addition of dppp (38 mg, 0.092 mmol) and DMF (3 mL) under CO (pCO = 6 atm, 140 °C, 72 h). The crude product was purified by chromatography (hexanes/EtOAc 9:1) to give, in order of elution, 35 (28 mg, 0.10 mmol, 24%, *Rf* = 0.88) as a yellow-orange solid and 53 (68 mg, 0.28 mmol, 67%, *Rf* = 0.58) as a yellow solid.

Analytical data for 53: mp = 89–90 °C; IR (ATR) 3395, 3056, 2978, 1600, 1545, 1496, 1461, 1436, 1413, 1327, 1253, 1186, 1070, 978, 914, 807, 767, 744, 704, 658 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.94 (br s, 1H), 7.54 (d, J = 8.4 Hz, 1H), 7.49–7.44 (m, 4H), 7.33–7.30 (m, 2H), 7.07 (dd, J = 9.0, 1.8 Hz, 1H), 2.50 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 135.5, 134.8, 132.1, 129.3, 128.6, 127.2, 126.4, 126.1, 120.5, 119.6, 114.6, 110.3, 12.4; HRMS (ESI, negative mode) m/z $[M-H]^-$ calcd for $C_{15}H_{11}ClN$: 240.0586; found: 240.0583.

N,N-Dimethyl-N′-(2-methyl-3-phenyl-1*H*-indolyl)urea (54). Following Procedure A, styrene 36 (88 mg, 0.34 mmol) was treated with CO (pCO = 6 atm) in the presence of $Pd(OAc)_2$ (7.7 mg, 0.034 mmol), dppp (28 mg, 0.068 mmol) and phen (6.2 mg, 0.034 mmol) in DMF (3 mL) at 120 °C for 72 h. The crude product was purified by chromatography (hexanes/EtOAc 2:8, R_f = 0.12) to give 54 (13 mg, 0.044 mmol, 13%) as a dark brown solid. mp = 247–248 °C; IR (ATR) 3452, 3268, 2918, 1647, 1591, 1524, 1463, 1422, 1369, 1207, 1193, 990, 798, 706 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (br s, 1H), 7.81 (d, J = 2.0 Hz, 1H), 7.52–7.40 (m, 5H), 7.29 (t, J = 7.2 Hz, 1H), 6.77 (dd, J = 8.4, 2.0 Hz, 1H), 6.37 (br s, 1H), 3.05 (s, 6H), 2.48 (s, 3H); $^{13}C\{^1H\}$ NMR (151 MHz $CDCl_3$ + DMSO-d_6) δ 156.0, 135.4, 135.2, 133.2, 130.9, 128.4, 127.7, 124.6, 123.0, 117.2, 113.5, 112.4, 102.7, 35.9, 11.9; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{18}H_{20}N_3O$: 294.1601; found: 294.1622.

Alternative synthesis: Following Procedure A, styrene 38 (60 mg, 0.21 mmol) was treated with $Pd(OAc)_2$ (4.7 mg, 0.021 mmol), dppp (17 mg, 0.041 mmol), phen (3.8 mg, 0.022 mmol) in DMF (3 mL) under CO (pCO = 6 atm, 120 °C, 72 h). The crude product was purified by chromatography (hexanes/EtOAc 2:8, R_f = 0.12) to give 54 (5.4 mg, 0.018 mmol, 9%) as a dark brown solid.

6-(*N*-Acetyl)amino-2-methyl-3-phenyl-1*H*-indole (55). Following Procedure A, styrene 37 (100 mg, 0.34 mmol) was treated with CO (pCO = 6 atm) in the presence of $Pd(OAc)_2$ (8.3 mg, 0.037 mmol), dppp (30 mg, 0.072 mmol) and phen (6.7 mg, 0.037 mmol) in DMF (3 mL) at 120 °C for 72 h. The crude product was purified by chromatography (hexanes/EtOAc 4:6, R_f = 0.15) to give 55 (76 mg, 0.29 mmol, 85%) as a pale yellow solid. mp = 250–251 °C; IR (ATR) 3329, 3259, 3049, 2913, 1628, 1560, 1533, 1493, 1464, 1419, 1370, 1264, 1195, 846, 795, 766, 708, 658 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$ and DMSO-d_6) δ 10.17 (br s, 1H), 9.15 (br s, 1H), 8.04 (d, J = 1.8 Hz, 1H), 7.51–7.46 (m, 3H), 7.43 (t, J = 7.20 Hz, 2H), 7.25 (t, J = 7.20 Hz, 1H), 6.94 (dd, J = 8.4, 1.8 Hz, 1H), 2.50 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$ and DMSO-d_6) δ 166.5, 134.2, 133.9, 131.6, 130.1, 127.1, 126.8, 123.5, 122.0, 116.0, 111.1, 111.0, 100.6, 22.5, 10.9; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{17}N_2O$: 265.1335; found: 265.1339.

Methyl 2-methyl-3-phenyl-1*H*-Indole-6-carboxylate (56). Following Procedure A, styrene 39 (60 mg, 0.20 mmol) was treated with CO (pCO = 6 atm) in the presence of $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), dppp (17 mg, 0.041 mmol) and phen (3.6 mg, 0.02 mmol) in DMF (3 mL) at 120 °C for 72 h. The crude product was purified by chromatography (hexanes/EtOAc 1:1, R_f = 0.56) to give 56 (19 mg, 0.07 mmol, 35%) as an off-white solid.

Following Procedure B, methyl 4-bromo-3-nitrobenzoate (27) (100 mg, 0.39 mmol) was treated with hydrazone 7 (175 mg, 0.58 mmol), $PdCl_2(PPh_3)_2$ (6.8 mg, 0.01 mmol), lithium *tert*-butoxide (116 mg, 1.45 mmol) in 1,4-dioxane (8 mL) at 100 °C for 1 h, followed by addition of dppp (32 mg, 0.078 mmol) under CO (pCO = 6 atm, 140 °C, 72 h). The crude product was purified by chromatography (hexanes/EtOAc 1:1, R_f = 0.56) to give 56 (32 mg, 0.12 mmol, 31%) as an off-white solid. mp = 195–196 °C; IR (ATR) 3324, 3088, 2950, 1687, 1624, 1508, 1434, 1359, 1283, 1274, 1218, 1129, 1092, 998, 874, 775, 743, 704, 670 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 8.20 (br s, 1H), 8.09 (s, 1H), 7.80 (d, J = 9.0 Hz, 1H), 7.65 (d, J = 9.0 Hz, 1H), 7.51–7.46 (m, 4H), 7.33 (tt, J = 6.6, 4.0 Hz, 1H), 3.94 (s, 3H), 2.55 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 168.3, 135.4, 134.7, 134.5, 131.5, 129.4, 128.6, 126.2, 123.0, 121.1, 118.2, 115.2, 112.6, 51.9, 12.7; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{16}NO$: 266.1176; found: 266.1189.

2-Propyl-3-phenyl-1*H*-indole (57). Following Procedure A, styrene 40 (80 mg, 0.30 mmol) was treated with CO (pCO = 6 atm) in the presence of $Pd(OAc)_2$ (6.7 mg, 0.03 mmol) was treated with dppp (28 mg, 0.068 mmol), phen (5.4 mg, 0.03 mmol) in DMF (3 mL) at 120 °C for 72 h. The crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.63) to give 57 (64 mg, 0.27 mmol, 90%) as a yellow solid. mp = 69–70 °C; IR (ATR) 3403, 3055, 2959, 2929, 2870, 1602, 1495, 1458, 1432, 1329, 1256, 1186, 1115, 986, 770, 741, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (br s, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.52–7.42 (m, 4H), 7.37–7.28 (m, 2H),

7.17 (tt, J = 6.8, 1.2 Hz, 1H), 7.10 (tt, J = 8.0, 1.2 Hz, 1H), 2.84 (t, J = 7.2 Hz, 2H), 1.73 (sextet, J = 7.6 Hz, 2H), 0.97 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 135.9, 135.4, 135.2, 129.6, 128.4, 127.9, 125.9, 121.5, 119.8, 118.9, 114.5, 110.3, 28.4, 23.1, 13.9.

3-(4-Methoxyphenyl)-2-methyl-1*H*-indole (58) [43]. Following Procedure A, styrene 41 (73 mg, 0.27 mmol) was treated with CO (pCO = 6 atm) in the presence of $Pd(OAc)_2$ (6.1 mg, 0.027 mmol), dppp (22 mg, 0.053 mmol), phen (4.9 mg, 0.028 mmol) in DMF (3 mL) at 120 °C for 72 h. The crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.58) to give 58 (49 mg, 0.21 mmol, 78%) as a pale yellow solid. mp = 123–124 °C; IR (ATR) 3347, 3054, 3007, 2910, 2835, 1563, 1509, 1457, 1283, 1236, 1173, 1106 1022, 986, 829, 815, 746, 671 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (br s, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.43 (d, J = 8.8 Hz, 2H), 7.33 (d, J = 8.0 Hz, 1H), 7.16 (td, J = 8.4, 0.8 Hz, 1H), 7.10 (td, J = 6.8, 1.2 Hz, 1H), 7.02 (d, J = 8.8 Hz, 2H) 3.87 (s, 3H), 2.49 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 157.8, 135.1, 131.0, 130.4, 128.0, 127.8, 121.4, 119.8, 118.7, 114.0, 114.0, 110.2, 55.3, 12.4.

3-(2,4-Dimethoxyphenyl)-2-methyl-1*H*-indole (6) [25]. Following procedure A, styrene 5 (81 mg, 0.27 mmol) was treated with CO (pCO = 6 atm) in the presence of $Pd(OAc)_2$ (6.1 mg, 0.027 mmol), dppp (22 mg, 0.053 mmol), phen (4.9 mg, 0.027 mmol) in DMF (3 mL) at 120 °C for 72 h. The crude product was purified by chromatography (hexanes/EtOAc 7:3, R_f = 0.43) to give 6 (42 mg, 0.16 mmol, 59%) as an off-white solid.

Following Procedure B, 2-bromonitrobenzene (16) (100 mg, 0.50 mmol) was treated with hydrazone 4 (269 mg, 0.74 mmol), $PdCl_2(PPh_3)_2$ (8.7 mg, 0.012 mmol), lithium *tert*-butoxide (149 g, 1.86 mmol) in 1,4-dioxane (8 mL) at 100 °C for 8 h, followed by addition of dppp (41 mg, 0.10 mmol) under CO (pCO = 6 atm, 140 °C, 72 h). The crude product was purified by chromatography (hexanes/EtOAc 7:3, R_f = 0.43) to give 6 (109 mg, 0.41 mmol, 82%) as an off-white solid. mp = 198–199 °C; IR (ATR) 3387, 2999, 2958, 2934, 2834, 1612, 1566, 1503, 1459, 1302, 1258, 1209, 1158, 1136, 1049, 1032, 826, 797, 747, 599, 584, 543, 519 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (br s, 1H), 7.39 (d, J = 8.0 Hz, 1H), 7.32–7.27 (m, 2H), 7.11 (td, J = 6.8, 1.2 Hz, 1H), 7.05 (td, J = 7.2, 0.8 Hz, 1H), 6.62–6.58 (m, 2H), 3.88 (s, 3H), 3.78 (s, 3H), 2.36 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.7, 158.3, 135.2, 132.5, 132.3, 128.7, 121.0, 119.4, 119.2, 116.5, 110.2, 110.2, 104.3, 99.0, 55.4, 55.4, 12.7.

6,7-Dihydro-5*H*-benzo[*c*]carbazole (59) [44]. Following Procedure A, styrene 42 (80 mg, 0.32 mmol) was treated with CO (pCO = 6 atm) in the presence of $Pd(OAc)_2$ (7.1 mg, 0.032 mmol), dppp (22 mg, 0.063 mmol), phen (5.7 mg, 0.032 mmol) in DMF (3 mL) at 120 °C for 72 h. The crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.23) to give 59 (50 mg, 0.23 mmol, 72%) as an off-white solid. mp = 103–104 °C; IR (ATR) 3404, 3049, 2930, 2893, 2831, 1601, 1548, 1496, 1447, 1355, 1254, 1183, 1015, 968, 742, 733, 693 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (dd, J = 7.2, 1.2 Hz, 1H), 7.97 (br s, 1H), 7.85 (dd, J = 7.2, 1.2 Hz, 1H), 7.38–7.27 (m, 2H), 7.24–7.15 (m, 3H), 7.08 (td, J = 7.2, 1.6 Hz, 1H), 3.06 (t, J = 8.0 Hz, 2H), 2.99–2.91 (m, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 137.2, 136.1, 133.8, 133.3, 127.9, 126.9, 124.9, 124.3, 122.2, 121.4, 120.5, 119.4, 111.1, 110.6, 29.4, 22.4.

5,6-Dihydro-3-methylindeno[2,1-*b*]indole (60). Following Procedure A, styrene 43 (67 mg, 0.27 mmol) was treated with CO (pCO = 6 atm) in the presence of $Pd(OAc)_2$ (5.9 mg, 0.027 mmol), dppp (22 mg, 0.053 mmol), phen (4.8 mg, 0.027 mmol) in DMF (3 mL) at 120 °C for 72 h. The crude product was purified by chromatography (hexanes/EtOAc 8:2, R_f = 0.17) to give 60 (26 mg, 0.12 mmol, 44%) as a black solid. mp = 214–215 °C; IR (ATR) 3374, 3056, 2915, 1616, 1574, 1483, 1449, 1385, 1248, 1215, 1168, 1021, 818, 736, 725 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 11.48 (br s, 1H), 7.82–7.79 (m, 1H), 7.51 (d, J = 7.6 Hz, 1H), 7.44–7.40 (m, 1H), 7.25 (s, 1H), 7.12–7.06 (m, 3H), 3.76 (s, 2H), 2.34 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 147.2, 143.4, 141.0, 137.5, 131.2, 127.5, 126.2, 121.8, 121.0, 120.3, 119.8, 119.0, 117.9, 112.6, 31.0, 21.5; HRMS (ESI, negative mode) m/z $[M - H]^-$ calcd for $C_{16}H_{12}N$: 218.0975; found: 218.0971.

3-(3-Pyridinyl)-1*H*-indole (61) [45]. Following procedure A, styrene 44 (90 mg, 0.40 mmol) was treated with CO (pCO = 6 atm) in the presence of $Pd(OAc)_2$ (8.9 mg, 0.04 mmol), dppp (33 mg, 0.04 mmol), phen (7.2 mg, 0.04 mmol) in DMF (3 mL) at 120 °C for 72 h. The crude product was purified by chromatography (hexanes/EtOAc 3:7, R_f = 0.23) to give 61 (76 mg, 0.39 mmol, 98%) as a yellow gum. IR (ATR) 3400, 3038, 2972, 2922. 1565, 1539, 1456, 1408, 1338, 1308, 1242, 1125, 962, 800, 738, 707 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.94 (dd, J = 2.4, 0.8 Hz, 1H), 8.57 (br s, 1H), 8.53 (dd, J = 3.6, 1.6 Hz, 1H), 7.98 (ddd, J = 8.0, 2.3, 1.7 Hz, 1H), 7.90 (ddt, J = 7.8, 1.4, 0.8 Hz, 1H), 7.47 (td, J = 8.0, 0.8 Hz, 1H), 7.44 (d, J = 2.8 Hz, 1H), 7.37 (ddd, J = 8.0, 4.8, 0.8 Hz, 1H), 7.29 (td, J = 7.2, 0.8 Hz, 1H), 7.23 (td, J = 8.4, 1.6 Hz, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 148.1, 146.6, 136.8, 134.5, 131.9, 125.4, 123.7, 122.6, 122.5, 120.6, 119.2, 114.1, 111.7.

1,3,4,9-Tetrahydrospiro[2*H*-carbazole-2,2'-[1,3]dioxolane] (62) [46]. Following Procedure A, styrene 45 (84 mg, 0.32 mmol) was treated with CO (pCO = 6 atm) in the presence of $Pd(OAc)_2$ (7.3 mg, 0.032 mmol), dppp (27 mg, 0.065 mmol), phen (5.8 mg, 0.032 mmol) in DMF (3 mL) at 120 °C for 72 h. The crude product was purified by chromatography (hexanes/EtOAc 7:3, R_f = 0.45) to give 62 (60 mg, 0.26 mmol, 81%) as a pale yellow solid. mp = 89–90 °C; IR (ATR) 3398, 2924, 2893, 2851, 1600, 1467, 1452, 1284, 1236, 1099, 1057, 1011, 946, 840, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.68 (br s, 1H), 7.46 (d, J = 7.6 Hz, 1H), 7.27 (d, J = 6.8 Hz, 1H), 7.14–7.05 (m, 2H), 4.06 (s, 4H), 3.00 (s, 2H), 2.89 (t, J = 6.4 Hz, 2H), 2.04 (t, J = 6.4 Hz, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 136.4, 131.4, 127.1, 121.2, 119.2, 118.0, 110.5, 109.1, 109.0, 64.7, 64.7, 34.3, 32.0, 18.8.

7-Aza-3-phenylindole (63) [25], 1-Hydroxy-4-phenyl-1,8-naphthyridin (64) [47] and 2-Amino-3-(1-phenyl-1-ethenyl-1-yl) pyridine (65). Following procedure A, styrene 46 (79 mg, 0.35 mmol) was treated with CO (pCO = 6 atm) in the presence of $Pd(OAc)_2$ (7.8 mg, 0.035 mmol), dppp (29 mg, 0.07 mmol), phen (6.3 mg, 0.035 mmol) in DMF (3 mL) at 120 °C for 72 h . The crude product was purified by chromatography (hexanes/EtOAc 1:1) to give 63 containing a trace amount of 65 (46 mg, 0.24 mmol, 69%, 63/65–20:1, R_f = 0.30) followed by 64 (14.3 mg, 0.063 mmol, 18%, R_f = 0.20), both as white solids.

7-Aza-3-phenylindole (63), 2-Nitro-3-(1-phenyl-1-ethene-1-yl) pyridine (46) and 2-Amino-3-(1-phenyl-1-ethene-1-yl)pyridine (65). Following Procedure B, 3-bromo-1-nitropyridine (28) (100 mg, 0.493 mmol) was treated with acetophenone 4-methylphenylsulfonylhydrazone (14) [24] (213 mg, 0.74 mmol) in the presence of $PdCl_2(PPh_3)_2$ (8.7 mg, 0.012 mmol) and Li*Ot*-Bu (148 mg, 1.85 mmol) in 1,4-dioxane (8 mL) at 100 °C for 1 h, followed by addition of dppp (40.7 mg, 0.10 mmol) under CO (pCO = 6 atm, 140 °C, 72 h). The crude product was purified by chromatography (hexanes/EtOAc, 7:3 then 1:1) to give, in order of elution, 46 (21.9 mg, 0.097 mmol, 20%, R_f = 0.70) as a brown oil and a mixture of 63 and 65 (69.0 mg, R_f = 0.30). The two compounds were separated by a second chromatography (hexanes/EtOAc/acetic acid, 7:3:0.1) to give 63 as a mixture with acetic acid. In order to elute compound 65, the mobile phase was changed (hexanes/EtOAc, 6:4) and 65 (11.9 mg, 0.061 mmol, 12%) was isolated as a faint brown solid. Acetic acid was removed from the mixture with 63 by a third chromatography (hexanes/EtOAc, 7:3 then 1:1) to give pure 63 (57.1 mg, 0.294 mmol, 60%) as a white solid.

Analytical data for 63: mp = 188–189 °C; IR (ATR) 3082, 3030, 2988, 2875, 1533, 1418, 1264, 960, 895, 771, 697, 750 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 11.91 (br s, 1H), 8.31–8.26 (m, 2H), 7.87 (d, J = 2.4 Hz, 1H), 7.72 (d, J = 7.2 Hz, 2H), 7.44 (t, J = 8.0 Hz, 2H), 7.26 (t,

$J = 7.6$ Hz, 1H), 7.16 (dd, $J = 7.2$, 4.4 Hz, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 149.1, 142.9, 135.1, 128.9, 127.5, 126.3, 125.7, 123.7, 117.3, 116.1, 114.3.

Analytical data for 64: mp = 263–264 °C; IR (ATR) 1645, 1590, 1376, 758, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.89 (br s, 1H), 8.59 (dd, $J = 4.7$, 1.6 Hz, 1H), 7.90 (dd, $J = 8.3$, 1.8 Hz, 1H), 7.56–7.51 (m, 3H), 7.46–7.42 (m, 2H), 7.16 (dd, $J = 8.3$, 5.0 Hz, 1H), 6.68 (s, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 162.2, 150.7, 150.4, 150.1, 135.7, 134.9, 129.1, 128.9, 128.8, 122.2, 118.4, 113.7.

Analytical data for 65: mp = 97–98 °C; IR (ATR) 3472, 3135, 2920, 1568, 1442, 1418, 1282, 771, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (dd, $J = 5.2$, 1.2 Hz, 1H), 7.42–7.30 (m, 6H), 6.72 (dd, $J = 7.6$, 5.2 Hz, 1H), 5.80 (s, 1H), 5.39 (s, 1H), 4.50 (br s, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 156.0, 147.3, 145.9, 138.6, 138.6, 128.8, 128.5, 126.6, 121.6, 117.0, 114.0; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{13}H_{13}N_2$: 197.1073; found: 197.1071.

1,2,3,4-Tetrahydrocarbazole (66) [48]. Following Procedure B, 2-bromonitrobenzene (16) (100 mg, 0.50 mmol) was treated with hydrazone 15 (198 mg, 0.74 mmol), $PdCl_2(PPh_3)_2$ (8.7 mg, 0.012 mmol), lithium *tert*-butoxide (149 g, 1.86 mmol) in 1,4-dioxane (8 mL) at 100 °C for 15 h; followed by addition of dppp (41 mg, 0.10 mmol) under CO (pCO = 6 atm, 140 °C, 72 h). The crude product was purified by chromatography (hexanes/EtOAc 8:2, $R_f = 0.61$) to give 66 (55 mg, 0.32 mmol, 64%) as an off-white solid. mp = 113–114 °C; IR (ATR) 3398, 2928, 2848, 1469, 1304, 1234, 1144, 738 cm-1; ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (br s, 1H), 7.46 (d, $J = 7.2$ Hz, 1H) 7.29–7.26 (m, 1H), 7.13–7.04 (m, 2H), 2.76–2.68 (m, 4H), 1.96–1.83 (m, 4H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 135.6, 134.1, 127.8, 120.9, 119.0, 117.7, 110.3, 110.1, 23.3, 23.2, 23.2, 20.9.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests. Bjorn Soderberg reports financial support was provided by National Institute of Health

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tet.2021.132331.

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