Palladium-Catalyzed Synthesis of Indoles by Reductive *N*-Heteroannulation of 2-Nitrostyrenes

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A palladium−phosphine catalyzed reductive *N*-heteroannulation of 2-nitrostyrenes, in the presence of carbon monoxide, producing indoles has been developed. Indoles were obtained, in moderate to excellent yield, from substituted 2-nitrostyrenes having either electron-withdrawing (NO_2 and CO_2-Me) or electron-donating (Br, OH, Me, OMe, and OTf) substituents on the aromatic ring. Best results were obtained using palladium diacetate (6 mol %) together with triphenylphosphine (24 mol %) as the catalytic system, under 4 atm of carbon monoxide in acetonitrile at 70 °C. Other palladium(II) and palladium(0) complexes also catalyze the reaction.

Introduction

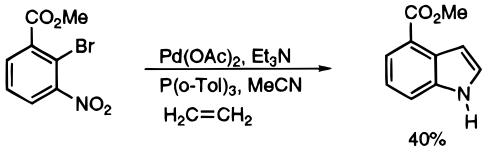
Since the first synthesis of indole by Bayer in 1866,[1] more synthetic routes to indoles have probably been published compared to any other heterocyclic, or carbocyclic, ring system.[2] A number of named reactions can be found in most heterocyclic chemistry textbooks, such as the Fischer, Madelung, Bischler, Reissert, Nenitzescu, and Leimgruber−Batcho indole syntheses, to name a few of the more well-known methods. More recently, several synthetic methods to highly substituted indole derivatives, employing transition metal reagents, have been developed.[3] Especially noteworthy are the numerous palladium-catalyzed routes employing, for example, 2-alkenylanilines, 2-alkynylanilines, 2-halo-*N*-alkenylanilines, and 2-halo-*N*-allylanilines.[4]

We have recently described a novel synthesis of indoles and quinolines, *via* a thermally induced intramolecular cyclization of *N*-aryl amino substituted Fischer chromium carbene complexes having a pendant vinyl substituent on the aryl group.[5] During this study, a number of substituted 2-vinylanilines and their nitrobenzene precursors were required for the synthesis of the carbene complexes. Upon an attempted methoxycarbonylation[6] of 3-bromo-2-ethenylnitrobenzene (**1**), using a catalytic amount of palladium diacetate and 1,3-bis(diphenylphosphino)propane, in the presence of triethylamine and carbon monoxide (4 atm) in a methanol−DMF solvent mixture, we were surprised to isolate 4-bromoindole (**2**) in 63% yield as the sole product (Scheme 1).[7] A few cases of a similar reaction were first observed by Kasahara *et al.* upon Heck reactions of 2-bromonitrobenzenes with ethene in the presence of palladium diacetate. For example, methyl indole-4-carboxylate was obtained by reaction of methyl 2-bromo-3-nitrobenzoate with ethene (Scheme 2).[8] Recently, Watanabe *et al.* published a related procedure employing 2-ethenyl-1-nitrobenzenes as starting materials using a catalytic amount of $PdCl_2(MeCN)_2$ in the presence of carbon monoxide, triphenylphosphine, and an excess of tin dichloride (Scheme 3).[9] A few other reductive cyclization reactions, related to those shown in Schemes 1 and 3, can be found in the literature. Indoles, in addition to a number of side

Scheme 1

1 **2** (63%)

Scheme 2



40%

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[⊗] Abstract published in *Advance ACS Abstracts,* July 15, 1997.

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(7) Presented in part at the 211th American Chemical Society meeting, New Orleans, 1996, Abstract ORGN-86.

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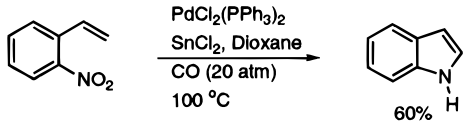
Scheme 3



products, have been prepared by reaction of 2-nitrostyrenes with a catalytic amount of various metal carbonyls[10] and palladium(II) salts[11] at high pressure and temperature. 2-Aryl-4-quinolinones can be obtained from 2-nitrochalcones *via* ruthenium(0)- or palladium(II)-catalyzed reactions in the presence of carbon monoxide (30 atm, 170 °C).[12] In addition, syntheses of quinazolines[13] and 1-pyrroline derivatives[14] have been reported employing a variety of transition metal catalysts. Finally, McMurry type cyclizations of aromatic acylamido carbonyl compounds forming indoles have been described.[15] Reductive cyclization can also be obtained in the absence of a transition metal catalyst and carbon monoxide. Sundberg has reported a reaction using excess triethylphosphite as the reducing agent at elevated temperatures.[16]

Compared to Watanabe's procedure, our protocol proceeds at a substantially lower temperature and pressure and does not require an added Lewis acid, such as tin dichloride. It should also be noted that in the latter study only substitution on the pendant alkene was examined. Compared to previously reported palladium-catalyzed routes to indoles employing aniline derivatives, this route offers some one or more of the following advantages: (1) no protection group strategies are required, (2) nitrobenzenes are usually the precursors to the aniline derivatives, thus eliminating additional synthetic steps, and (3) no re-oxidant, such as 1,4-benzoquinone, is required. Thus, the present method potentially offers a shorter, milder, and more economical route to substituted indoles. With this in mind, an in-depth study of this reductive *N*-heteroannulation reaction was undertaken. Herein is reported the scope and limitation of this method.

Results and Discussion

The reaction conditions for the reaction of **1** forming **2** were studied in more detail, and the results thereof are summarized in Table 1. Three of the reagents were shown to be crucial for the formation of **2**; only starting material was recovered from reactions of **1** in the absence of either phosphine, palladium catalyst, or carbon monoxide (entries 2−4). A small decrease in yield was observed when a somewhat higher carbon monoxide pressure was employed (entry 5). In contrast, the yield dropped significantly at 1 atm of carbon monoxide, and a substantial amount of starting material was recovered after 22 h (entry 6). An insignificant increase in yield, compared to entry 6, could be realized when the reaction was performed at 120 °C (entry 7). Neither methanol nor triethylamine, used in our preliminary experiment, is required for the reaction to proceed (entries 8 and 9). In fact, the reaction rate appears to be somewhat faster in the absence of triethylamine. In addition to the DMF−methanol solvent mixture, the three solvents examined—methanol, DMF, and acetonitrile—gave satisfactory yields of **2**. Since, the reactions performed in acetonitrile appeared to be somewhat cleaner and easier to workup, it was the solvent of choice (entry 14). A number of different palladium reagents can be used as catalysts. Palladium(II) salts, such as $Pd(OAc)_2$, and $PdCl_2(MeCN)_2$, and palladium(0) reagents, such as $Pd(dba)_2$ and Pd/C (10% Pd), all enter the catalytic cycle, forming **2** under various reaction conditions (entries 15−20).

Methyl *N*-(3-bromo-2-ethenylphenyl)carbamate (**3**, ≤17%) and methyl 2-ethenyl-3-nitrobenzoate (**15**, ≤11%), the originally expected product, were the only side products isolated from reaction of **1**. Carbamates and urea derivatives have previously been prepared by reduction of aromatic nitro compounds in methanol using a palladium−phosphine catalyst at high carbon monoxide pressure (40−80 atm).[17] For obvious reasons, these two products are observed only in the presence of methanol; no additional or related side products have been isolated using DMF or acetonitrile as the solvent in the absence of methanol. A 17% yield of **3** was realized in the absence of triethylamine. This may open a new palladium-catalyzed route to carbamates. The highest yield of the ester **15** was obtained using only 1 equiv of triphenylphosphine to palladium, a side reaction that was completely eliminated by employing 4 equiv of phosphine (entries 10 and 11). Further reaction of 4-bromoindole (**2**) to methyl 4-indolecarboxylate (**32**) was not observed. This result is intriguing in that a palladium-catalyzed carbomethoxylation of **2** under similar reaction conditions, using $PdBr_2(PPh_3)_2$ as the catalyst, has previously been reported.[18]

For the present synthesis, the overall yield of 4-bromoindole (**2**) compares favorably to previously published routes. For example, using the same starting material, the overall yield of 4-bromoindole (**2**) following our protocol (82%) is higher compared to the yield obtained from a Leimgruber-Batcho reaction (70%)[19] and substantially higher compared to Hegedus's palladium (II)-catalyzed reaction[20] (≤50%). A fourth route to 4-bromoindole starting from 3-bromo-2-methylnitrobenzene *via* 3-bromo-2-(2-hydroxyethenyl)nitrobenzene has been published (≤72%).[21]

To determine the scope of the reaction and to evaluate the influence of substituents on the alkene and the aromatic ring, a number of substituted 2-nitrostyrenes were prepared. The alkenyl group was introduced either

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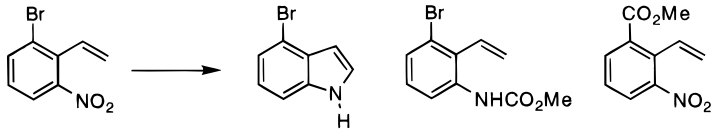
Table 1. Reaction Condition Study

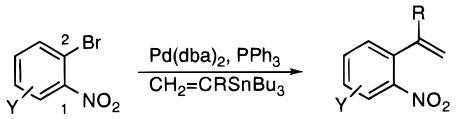


1 **2** **3** **15**

entry[a]	catalyst	phosphine	solvent	base	atmosphere	yield (%)[b,c] **2**	**3**	**15**
1	$Pd(OAc)_2$	dppp[d]	DMF−MeOH	NEt_3	CO	63 (68)		trace[e]
2	$Pd(OAc)_2$		DMF-MeOH	NEt_3	CO	*f*		trace
3		dppp	DMF-MeOH	NEt_3	CO	*f*		
4	$Pd(OAc)_2$	dppp	DMF-MeOH	NEt_3	Ar (3 atm)	*f*		
5	$Pd(OAc)_2$	dppp	DMF-MeOH	NEt_3	CO (6 atm)	56 (58)	3	
6	$Pd(OAc)_2$	dppp	DMF-MeOH	NEt_3	CO (1 atm)	22 (69)		8
7	$Pd(OAc)_2$	dppp	DMF-MeOH	NEt_3	CO (1 atm)[g]	27 (53)[h]		
8	$Pd(OAc)_2$	dppp	DMF	NEt_3	CO	59 (89)		
9	$Pd(OAc)_2$	dppp	DMF-MeOH		CO	76	17	
10	$Pd(OAc)_2$	PPh_3[i]	DMF-MeOH	NEt_3	CO	76 (85)		11
11	$Pd(OAc)_2$	PPh_3	DMF-MeOH	NEt_3	CO	86		
12	$Pd(OAc)_2$	PPh_3	DMF		CO	76 (82)		
13	$Pd(OAc)_2$	PPh_3	MeCN-MeOH	NEt_3	CO	80		
14	$Pd(OAc)_2$	PPh_3	MeCN[j]		CO	84		
15	$Pd(dba)_2$	dppp	DMF-MeOH	NEt_3	CO	49 (89)	trace	6
16	$PdCl_2(MeCN)_2$	dppp	DMF-MeOH	NEt_3	CO	82	8	
17	$PdCl_2(MeCN)_2$	PPh_3	MeCN		CO	47 (90)		
18	Pd/C (10%)	dppp	DMF-MeOH	NEt_3	CO	45 (61)	trace	3
19	Pd/C (10%)	dppp	DMF		CO[k]	56 (76)		
20	Pd/C (10%)	PPh_3	MeOH		CO	56 (63)		

[a] All reactions were performed at 70 °C (oil bath temperature) for 22 h using 2 mmol of **1**, 6 mol % catalyst, 6 mol % phosphine for dppp or 24 mol % for PPh_3 dissolved in 6 mL of DMF−MeOH (2:1) under 4 atm of CO, unless otherwise stated. [b] Pure isolated compounds after column chromatography. [c] Yield in parentheses is based on recovered starting material. [d] dppp = 1,3-bis(diphenylphosphino)propane. [e] Trace <3% by ^{1}H NMR of the crude reaction mixture. [f] Only starting material was observed by ^{1}H NMR of the crude reaction mixture. [g] At 120 °C (oil bath temperature) for 22 h. [h] A complex inseparable mixture of products containing some starting material and **13** was also isolated. [i] 6 mol % phosphine was used. [j] Heated for 15 h. [k] Heated for 48 h.

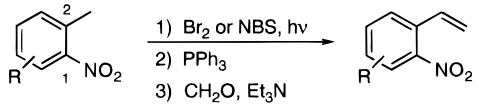
Table 2. Cross-Coupling of 2-Bromonitrobenzenes



entry[a]	Y	R	yield (%)[b]
1	4-Me	H	**8** (78)
2	3-OMe	H	**9** (89)
3	4-OMe	H	**10** (61)
4	5-OMe	H	**11** (96)
5	5-OMe	Me	**12** (79)[c]
6	3-OH	H	**13** (30)
7	5-CO_2Me	H	**17** (52)[d]
8	4-Br	H	**19** (81)[d]

[a] See Experimental Section for details. [b] Isolated pure products. [c] Tetrakis(triphenylphosphine)palladium(0) was used. [d] 2-OTf was used in place of 2-Br, and LiCl was added to the reaction mixture.

Table 3. Styrene Synthesis *via* the Wittig Reaction



entry[a]	R	bromide	yield (%)[b] Wittig salt	alkene
1	3-Br			**1** (95)[c]
2	3-CO_2Me		99[d]	**15** (92)
3	4-CO_2Me	55	95	**16** (99)
4	6-CO_2Me	55	75	**18** (100)
5	3-NO_2	79	90	**20** (91)

[a] See Experimental Section for details. [b] The yields for the bromides and the Wittig salts are crude yields, and the yields for the alkenes are for pure isolated compounds. [c] Overall yield for three steps. A modification of the reaction reported in ref 20 (83%) was used. [d] Yield for two steps.

by a palladium-catalyzed cross coupling of 1-alkenyl tri-*n*-butyltin derivatives with aryl bromides or triflates (Stille coupling) or by Wittig olefination. Coupling reactions[22] of bromo-, carbomethoxy-, methoxy-, and methyl-substituted 2-bromonitrobenzene with ethenyl- or 2-(1-propenyl)tri-*n*-butyltin proceeded uneventfully, and the corresponding 2-vinylnitrobenzene derivatives were obtained in good to excellent yield (Table 2). Coupling of 3-hydroxy-2-bromonitrobenzene (entry 6) gave a low yield of 2-ethenyl-3-hydroxynitrobenzene (**13**). Although low, the yield is satisfactory since Stille *et al*. reported that no reaction was observed from the related 2-bromo-3-hydroxy-*N*-tosylaniline (entry 3).[23,24]

Several phosphonium salts were prepared from the corresponding 2-methyl-1-nitrobenzenes *via* radical bromination and reaction with triphenyl phosphine. Wittig reactions of these benzylic phosphonium salts with formaldehyde gave the expected alkenes in excellent yield (Table 3).

Next, with a number of substituted 2-(1-alkenyl)-1-nitrobenzenes in hand, we examined the cyclization reaction using the optimized reaction conditions in Table 1 (entry 14). The results thereof are summarized in Table 4. Indole (**21**) and 2-phenylindole (**24**) were obtained in 87% and 100% yield, respectively (entries 1 and 4), yields substantially higher than those reported

(22) For a review on palladium-catalyzed cross-coupling reactions using organotin reagents, see: (a) Stille, J. K. *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 508. (b) Mitchell, T. N. Synthesis **1992**, 803.

(23) The presence of an hydroxy group is in itself not detrimental to the Stille reaction. (a) Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 5478. (b) Foote, K. M.; Hayes, C. J.; Pattenden, G. *Tetrahedron Lett.* **1996**, *37*, 275.

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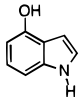
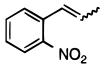
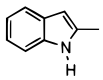
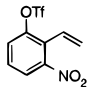
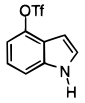
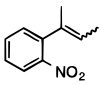
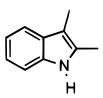
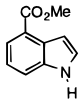
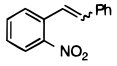
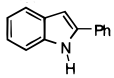
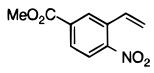
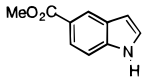
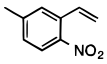
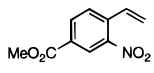
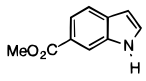
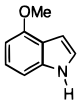
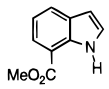
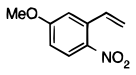
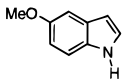
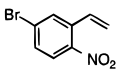
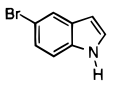
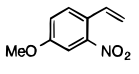
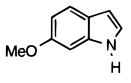
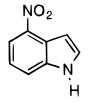
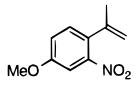
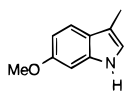
Table 4. Formation of Indoles From 2-Nitrostyrenes

Entry	Nitrobenzene[a]	Indole (Yield)[b]	Entry	Nitrobenzene[a]	Indole (Yield)[b]
1	 **4**	 **21** (87%)	10	 **13**	 **30** (96%)
2	 **5** (1:1, trans:cis)	 **22** (96%)	11	 **14**	 **31** (40%, 66%)[c]
3	 **6** (1:2, trans:cis)	 **23** (97%)	12	 **15**	 **32** (100%)
4	 **7** (trans only) **7** (1:1, trans:cis)	 **24** (100%) **24** (91%)	13	 **16**	 **33** (47%, 82%)[c]
5	 **8**	 **25** (51%)	14	 **17**	 **34** (78%, 80%)[c]
6	 **9**	 **26** (89%)	15	 **18**	 **35** (71%, 95%)[c]
7	 **10**	 **27** (63%)	16	 **19**	 **36** (0%)[d]
8	 **11**	 **28** (40%)	17	 **20**	 **37** (89%)
9	 **12**	 **29** (81%)			

[a] For reaction conditions, see Experimental Section. [b] Pure isolated compounds after column chromatography. [c] The second yield in parentheses is the yield based on recovered starting material. [d] Only starting material was isolated (89%).

by Watanabe *et al.*, who employed the same starting materials. The stereochemistry of the alkene does not affect the outcome of a given reaction. For example, no apparent rate or yield decrease was observed using a mixture of *cis*- and *trans*-2-nitrostilbene compared to pure *trans*-2-nitrostilbene (entries 2−4). In general, the reaction appears to be independent of the substitution pattern and electronic properties of the substituents on the aromatic ring. Substrates containing either electron-donating (entries 3−9) or electron-withdrawing (entries 10−13 and 16) groups react to give indoles in moderate to excellent yields. The reaction is very clean and, usually, only the expected indole was observed by ^{1}H NMR of the crude reaction mixtures. Reactions forming 4-substituted indoles are particularly successful, and yields ranging from 84% to 100% were realized, regardless of the electronic properties of the substrates. A hydroxy functionality in the 3-position of the substrate does not interfere with the reaction, and 4-hydroxyindole (**30**) can be isolated from **13** in almost quantitative yield (entry 8). It is interesting to note that only one of the nitro groups in **20** is reduced under the reaction conditions. Reduction of an additional nitro group is often observed using the Leimgruber−Batcho procedure.[25,26]

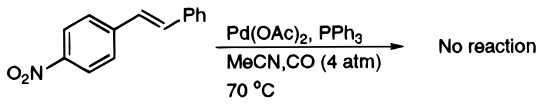
The synthetic sequence starting from methyl 2-methyl-3-nitrobenzoate (Table 2, entry 2) represents, to our knowledge, the best current alternative to methyl indole-4-carboxylate (**32**).[27] However, an exception is the reaction of the triflate **14**, where, in addition to the expected product 4-[(trifluoromethyl)sulphonyl]indole (**31**), a fair amount of starting material is recovered (entry 9). The relatively low isolated yield of 6-methoxyindole (**28**) is probably a reflection of the product's rapid oligomerization under the reaction conditions (entry 6). In this case, upon chromatography of the crude reaction mixture, a

(25) By careful control of stoichiometry of the reducing agent overreduction can be avoided: Somei, M.; Inoue, S.; Tokutake, S.; Yamada, F.; Kaneko, C. *Chem. Pharm. Bull.* **1981**, *29*, 726.

(26) For a recent method to 4-nitroindoles, see: Bergman, J.; Sand, P. *Tetrahedron* **1990**, *46*, 6085.

(27) (a) Ponticello, G. S.; Baldwin, J. J. *J. Org. Chem.* **1979**, *44*, 4003. (b) Kozikowski, A. P.; Ishida, H.; Chen, Y. Y. *J. Org. Chem.* **1980**, *45*, 3350.

Scheme 4



number of highly colored bands with high polarity were observed. The identity of these products has not been established. We anticipated a reduction of oligomerization in the presence of a 3-substituent on the formed indole. Thus, we were pleased to isolate 6-methoxy-3-methylindole (**29**) in 81% yield upon reaction of the 2-propenyl-substituted nitrobenzene **12** (entry 7).

One apparent difference between electron-donating and electron-withdrawing substituents is that the latter undergo cyclization at a somewhat slower rate. The esters **33**−**35** (and the triflate **31**) were isolated in fair to good yield together with varying amounts of starting material (entries 9 and 11−13). In the cases where starting material was recovered, a prolonged reaction time did not improve the chemical yield.

Although the mechanism for the reaction described herein and that reported by Watanabe *et al*. is closely related, it remains obscure. Based on a brief mechanistic study, formation of an active transition metal nitrene intermediate followed by an insertion reaction was suggested.[9] Since the reaction described by Izumi *et al*. proceeds in the absence of CO, a different mechanism is probably in operation. These authors tentatively suggested a mechanism consisting of an initial reduction of the nitro group to an amine, by an intermediately formed palladium hydride species, followed by a more conventional palladium(II)-catalyzed cyclization reaction producing the indole. In our case, the close proximity of the alkene to the nitro group was found to be crucial for the reaction to occur. For example, *trans*-4-nitrostilbene[28] was recovered unchanged, in quantitative yield, after 22 h (Scheme 4). This result is in sharp contrast to the quantitative yield of 2-phenylindole obtained from *trans*-2-nitrostilbene (Table 4, entry 4). It is plausible that palladium coordinated to the double bond assists in the reduction of the nitro group.

Finally, the only 2-nitrostyrene that did not undergo the cyclization reaction was **19**, which was recovered in 89% yield after 24 h (entry 14). No trace of the expected product, 5-bromoindole (**36**), was observed even after prolonged reaction time (5 days). We have presently no explanation for the lack of reactivity of **19**.

In conclusion, a relatively mild, palladium-catalyzed, reductive *N*-heteroannulation of 2-nitrostyrenes forming indoles in moderate to excellent yield has been developed. Applications of this methodology toward a number of naturally occurring indole alkaloids is presently underway in our laboratories.

Experimental Section

General Procedures. All NMR spectra were determined in $CDCl_3$ at 270 MHz (^1H NMR) and 67.5 MHz (^{13}C NMR) unless otherwise stated. The chemical shifts are expressed in δ values relative to Me_4Si (0.00, ^1H and ^{13}C) or $CDCl_3$ (7.26, ^1H and 77.00, ^{13}C) internal standards. Multiplicities observed in off-resonance decoupled ^{13}C NMR experiments are shown in parentheses. $^1H-^1H$ coupling constants are reported as calculated from spectra; thus, a slight difference between $J_{a,b}$ and $J_{b,a}$ is usually obtained. Results of APT (attached proton test) ^{13}C NMR experiments are shown in parentheses, where, relative to $CDCl_3$, (−) denotes CH_3 or CH and (+) denotes CH_2 or C.

Tetrahydrofuran (THF), 1,4-dioxane, toluene, and diethyl ether were distilled from sodium benzophenone ketyl prior to use. Pyridine, hexanes, acetonitrile, and ethyl acetate were distilled from calcium hydride. Chemicals prepared according to literature procedures have been footnoted the first time they are used; all other reagents were obtained from commercial sources and used as received. Silica gel (200−400 mesh) was used for flash chromatography. All reactions were performed in oven-dried glassware. Solvents were removed on a rotary evaporator at water aspirator pressure unless otherwise stated. Elemental analyses were performed by Atlantic Microlab, Inc., Norcross, GA.

2-Ethenyl-4-methylnitrobenzene (8).[8] To a solution of 2-bromo-4-methylnitrobenzene[29] (1.00 g, 4.61 mmol) and vinyltri-*n*-butyltin (1.61 g, 5.07 mmol) in toluene (25 mL) was added, under a positive flow of argon, bis(dibenzylideneacetone)palladium(0)[30] (265 mg, 0.46 mmol) together with triphenylphosphine (498 mg, 1.90 mmol). The solution was heated at reflux (19 h) whereupon a red solution containing a black precipitate was formed. The reaction mixture was cooled to ambient temperature, and the solvent was removed to give a black oil. The oil was dissolved in dichloromethane (50 mL), washed with NH_4OH (10%, aq, 3 × 30 mL), and dried ($MgSO_4$). Removal of solvent gave a yellow oil containing a smaller amount of a black viscous oil. The crude product was purified by chromatography (hexanes−EtOAc, 19:1) to give **8** (589 mg, 3.61 mmol, 78%) as a yellow oil.

2-Ethenyl-3-methoxynitrobenzene (9). A solution of 2-bromo-3-methoxynitrobenzene[24] (928 mg, 4.00 mmol) and vinyltri-*n*-butyltin (1.16 mL, 4.40 mmol) in toluene (30 mL) was reacted with bis(dibenzylideneacetone)palladium(0) (115 mg, 0.20 mmol) and triphenylphosphine (210 mg, 0.80 mmol) as described above (23.5 h). Extraction and purification by chromatography (hexanes−EtOAc, 19:1) gave **9** (641 mg, 3.58 mmol, 89%) as yellow crystals: mp 42−43 °C; ^1H NMR δ 7.83−6.98 (m, 3H), 6.71 (dd, J = 17.9 and 11.5, 1H), 5.68 (dd, J = 17.4 and 1.7 Hz, 1H), 5.52 (dd, J = 11.5 and 1.7 Hz, 1H), 3.86 (s, 3H); ^{13}C NMR δ 130.5 (s), 128.8 (d), 128.3 (d), 127.0 (s), 125.3 (s), 121.5 (t), 115.2 (d), 114.0 (d), 56.1 (q); IR (CH_2Cl_2) 2843, 1622, 1532, 1362, 1295, 1245, 1059 cm^{-1}. Anal. Calcd for $C_9H_9NO_2$: C, 60.33; H, 5.06. Found: C, 60.55; H, 5.15.

2-Ethenyl-4-methoxynitrobenzene (10).[8] A solution of 2-bromo-4-methoxynitrobenzene[31] (1.16 g, 5.00 mmol) and vinyltri-*n*-butyltin (1.45 mL, 5.50 mmol) in toluene (40 mL) was reacted with bis(dibenzylideneacetone)palladium(0) (144 mg, 0.25 mmol) and triphenylphosphine (263 mg, 1.00 mmol) as described above (46 h). Extraction and chromatography (hexanes−EtOAc, 19:1) gave 790 mg of a mixture of 2-ethenyl-4-methoxynitrobenzene and dibenzylideneacetone. The mixture was dissolved in THF (20 mL), and $NaBH_4$ (42 mg, 1.10 mmol) was added. After 20 h, the mixture was diluted with water (25 mL) and extracted with dichloromethane (3 × 25 mL). The combined organic phases were dried ($MgSO_4$) and filtered. The solvents were removed, and the residue was purified by chromatography (hexanes−EtOAc, 9:1) to give **10** (548 mg, 3.05 mmol, 61%) as faint yellow oil that crystallized upon storage in a freezer (−20 °C).

2-Ethenyl-5-methoxynitrobenzene (11).[8] A solution of 2-bromo-5-methoxynitrobenzene (2.32 g, 10.0 mmol) with vinyltri-*n*-butyltin (3.49 g, 11.0 mmol) in toluene (75 mL) was reacted with bis(dibenzylideneacetone)palladium(0) (288 mg, 0.50 mmol) and triphenylphosphine (525 mg, 2.00 mmol) as described above (24 h). Extraction and chromatography (hexanes−EtOAc, 9:1) gave **11** (1.72 g, 9.60 mmol, 96%) as a pale yellow oil.

5-Methoxy-2-propen-2-ylnitrobenzene (12). A similar reaction of 2-bromo-5-methoxynitrobenzene (4.64 g, 20.0 mmol)

(28) Aun, C. E.; Clarkson, T. J.; Happer, D. A. R. *J. Chem. Soc. Perkin Trans. 2* **1990**, 645.

(29) Coffey, S. *J. Chem. Soc.* **1926**, 3219.

(30) Takahashi, Y.; Ito, T.; Sakai, S.; Ishii, Y. *J. Chem. Soc., Chem. Commun*. **1970**, 1065.

(31) Hodgeson, H. H.; Moore, F. H. *J. Chem. Soc.* **1926**, 155.

with propen-2-yltri-*n*-butyltin[32] (6.62 g, 20.0 mmol) in toluene (100 mL) in the presence of tetrakis(triphenylphosphine)-palladium(0) (116 mg, 0.10 mmol) for 64 h gave, after extraction and chromatography (hexanes-EtOAc, 8:2), **12** (3.04 mg, 15.76 mmol, 79%) as a pale yellow oil: ^{1}H NMR δ 7.37 (d, J = 2.8 Hz, 1H), 7.23 (d, J = 8.5 Hz, 1H), 7.08 (dd, J = 8.5 and 2.6 Hz, 1H), 5.14 (t, J = 1.6 Hz, 1H), 4.90 (br s, 1H), 3.86 (s, 3H), 2.05 (s, 3H); ^{13}C NMR δ 158.6 (+), 148.4 (+), 142.4 (+) 131.2 (−), 130.9 (+), 118.8 (−), 114.9 (+) 108.6 (−), 55.6 (−), 23.1 (−); IR (neat) 1529; 1353 cm^{-1}. Anal. Calcd for $C_{10}H_{11}NO_3$: C, 62.17; H, 5.74. Found: C, 62.44; H, 5.74.

2-Ethenyl-3-hydroxynitrobenzene (13). A solution of 2-bromo-3-hydroxynitrobenzene[24] (2.18 g, 10.0 mmol) and vinyltri-*n*-butyltin (3.49 g, 11.0 mmol) in toluene (75 mL) was reacted with bis(dibenzylideneacetone)palladium(0) (288 mg, 0.50 mmol) and triphenylphosphine (525 mg, 2.00 mmol) as described above (17 h). Extraction and chromatography (hexanes−EtOAc, 9:1) gave **13** (0.51 g, 3.00 mmol, 30%) as golden crystals: mp 62−64 °C; ^{1}H NMR δ 7.50 (dd, J = 7.9 and 1.4 Hz, 1H), 7.27 (t, J = 8.1 Hz, 1H), 7.19 (dd, J = 8.1 Hz and 1.4 Hz, 1H), 6.84 (dd, J = 18.2 and 11.7 Hz, 1H), 6.43 (br s, 1H), 5.74 (dd, J = 11.7 and 1.4 Hz, 1H), 5.63 (dd, J = 18.0 and 1.2 Hz, 1H); ^{13}C NMR δ 153.9 (+), 148.6 (+), 129.0 (−), 128.6 (−), 122.0 (+), 120.7 (−), 119.8 (+), 116.2 (−); IR (CH_2Cl_2) 3464, 1519, 1360, 1293, 925 cm^{-1}. Anal. Calcd for $C_8H_7NO_3$: C, 58.18; H, 4.27. Found: C, 58.28; H, 4.34.

Methyl 2-ethenyl-3-nitrobenzoate (15). Bromine (2.77 mL, 54.0 mmol) dissolved in carbon tetrachloride (20 mL) was added over 30 min to a boiling solution of methyl 2-methyl-3-nitrobenzoate[27a] (8.83 g, 45.0 mmol) and dibenzoyl peroxide (543 mg, 2.25 mmol) in carbon tetrachloride (80 mL) under irradiation using a 100 W lamp. After 20 h of heating and irradiation,[33] additional bromine (0.69 mL, 13.5 mmol) in carbon tetrachloride (5 mL) and dibenzoyl peroxide (136 mg, 0.56 mmol) was added. After continued heating and irradiation (29 h), the red solution was allowed to cool to ambient temperature followed by solvent removal, affording crude methyl 2-bromomethyl-3-nitrobenzoate (12.8 g) as pale brown crystals. The crude product was used in the next reaction without further purification. Spectral data of the crude reaction mixture: mp 68−69 °C; ^{1}H NMR δ 8.09 (dd, J = 7.7 and 1.2 Hz, 1H), 7.94 (dd, J = 8.1 and 1.2 Hz, 1H), 7.53 (t, J = 8.1 Hz, 1H), 5.15 (s, 2H), 3.99 (s, 3H); ^{13}C NMR δ 165.8 (+), 150.5 (+), 134.7 (−), 132.5 (+), 132.3 (+), 129.1 (−), 127.7 (−), 53.0 (−), 22.7 (+); IR (neat) 1722, 1530, 1271 cm^{-1}. Anal. Calcd for $C_9H_8BrNO_4$: C, 39.44; H, 2.94. Found: C, 39.33; H, 2.94.

Triphenylphosphine (18.87 g, 49.5 mmol) was added to a solution of methyl 2-bromomethyl-3-nitrobenzoate (12.40 g, 44.12 mmol) in chloroform (60 mL). The solution was heated at reflux (1 h). After cooling to ambient temperature, dry diethyl ether (200 mL) was added to precipitate the Wittig salt. The slurry was cooled in a freezer (−20 °C) overnight followed by filtration to give a white powder. The powder was washed with dry diethyl ether (200 mL) and dried under high vacuum to give the crude phosphonium salt (23.42 g, 43.58 mmol, 99%). The salt was used as such without further purification.

Methanal (g) was bubbled through a purple solution of the salt (1.00 g, 1.86 mmol) and triethylamine (514 μL, 4.00 mmol) in dichloromethane (50 mL) at ambient temperature. Upon addition of methanal, the purple color of the ylide slowly changed to a pale brownish-yellow, which indicated the end point of the reaction. The solvent was removed, affording a yellowish-white crystalline residue. The crystalline mass, containing product and triphenylphosphine oxide, was added to a filter funnel and washed with hexanes (100 mL). The solvent was removed from the filtrate to give the crude product. Chromatography using hexanes−EtOAc (9:1) followed by hexanes−EtOAc (8:2) as eluent gave **15** (354 mg, 1.71 mmol, 92%) as pale yellow crystals: mp 41−42 °C; ^{1}H NMR δ 7.98 (dd, J = 7.7 and 1.2 Hz, 1H), 7.92 (dd, J = 8.3 and 1 Hz, 1H), 7.47 (t, J = 7.9 Hz, 1H), 7.18 (dd, J = 17.6 and 11.5 Hz, 1H), 5.43 (dd, J = 10.4 and 0.8 Hz, 1H), 5.23 (dd, J = 17.6 and 1.0 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR δ 166.1 (+), 149.8 (+), 133.3 (+), 132.6 (−), 132.5 (−), 131.5 (−), 127.6 (−), 125.9 (−), 118.9 (+), 52.1 (+); IR (neat) 1730, 1531, 1292, 1264, 1124, 707 cm^{-1}. Anal. Calcd for $C_{10}H_9NO_4$: C, 57.97; H, 4.38. Found: C, 57.72; H, 4.47.

Methyl 3-Ethenyl-4-nitrobenzoate (16).[8] A solution of methyl 3-methyl-4-nitrobenzoate[34] (3.92 g, 20.0 mmol), dibenzoyl peroxide (242 mg, 1.00 mmol), and *N*-bromosuccinimide (3.92 g, 22.0 mmol) in carbon tetrachloride (55 mL) was heated (90 °C, 22.5 h) and irradiated as described above. Solvent removal followed by chromatography (hexanes−EtOAc, 49:1) gave methyl 3-bromomethyl-4-nitrobenzoate (2.64 g, 9.61 mmol, 48%) as faint yellow crystals. Earlier fractions containing starting material, dibrominated product, and methyl 3-bromomethyl-4-nitrobenzoate were repurified by chromatography (hexanes−EtOAc, 9:1), affording an additional amount of product (400 mg, 1.45 mmol, 7%): mp 118−119 °C; ^{1}H NMR δ 8.23 (s, 1H), 8.12 (d, J = 8.4 Hz, 1H), 8.05 (d, J = 8.4 Hz, 1H), 4.82 (s, 2H), 3.97 (s, 3H); ^{13}C NMR δ 164.5 (+), 150.5 (+), 134.7 (−), 132.5 (+), 132.3 (+), 129.1 (−), 127.7 (−), 53.0 (−), 22.7 (+); IR (neat) 1720, 1529 cm^{-1}. Anal. Calcd for $C_9H_8BrNO_4$: C, 39.42; H, 2.94. Found: C, 39.57; H, 2.91.

Triphenylphosphine (2.10 g, 8.00 mmol) was reacted with methyl 3-bromomethyl-4-nitrobenzoate (2.00 g, 7.27 mmol) in chloroform (15 mL) as described above to give crude phosphonium salt (3.71 g, 6.90 mmol, ≤95%). The salt was used as such without further purification. Spectral data of the crude product: ^{1}H NMR δ 8.35 (s, 1H), 8.07 (d, J = 8.6 Hz, 1H), 7.93 (d, J = 8.6 Hz, 1H), 7.85−7.55 (m, 15H), 6.17 (d, J = 15.1 Hz, 2H), 3.83 (s, 3H).

A solution of the salt (3.00 g, 5.58 mmol) in dichloromethane (70 mL) was reacted with triethylamine (726 μL, 29.99 mmol) and methanal (g) as described above to give, after chromatography (hexanes−EtOAc, 9:1), **16** (1.14 g, 5.50 mmol, 99%) as pale yellow crystals.

Methyl 4-Ethenyl-3-nitrobenzoate (17).[8] To a solution of 4-carbomethoxy-2-nitrophenyl trifluoromethanesulfonate[4c] (1.98 g, 6.01 mmol) and vinyltri-*n*-butyltin (1.95 mL, 6.15 mmol) in dioxane (27 mL) was added, under a positive flow of argon, bis(dibenzylideneacetone)palladium(0) (70 mg, 0.12 mmol), triphenylphosphine (126 mg, 0.48 mmol), and LiCl (848 mg, 20.00 mmol), together with a few crystals of 2,6-(1,1-dimethylethyl)phenol. The solution was heated at reflux (20 h), whereupon a red solution containing a black precipitate was formed. The reaction mixture was cooled to ambient temperature, and the solvent was removed to give a black oil. The oil was dissolved in dichloromethane (50 mL), washed with NH_4OH (10%, aq, 3 × 50 mL) and H_2O (3 × 50 mL), and dried ($MgSO_4$). Removal of the solvent gave a brown oil that was purified by chromatography using hexanes−EtOAc (9:1) as eluent to give **17** (651 mg, 3.13 mmol, 52%) as yellow crystals.

Methyl 3-Ethenyl-2-nitrobenzoate (18).[8] A solution of methyl 3-methyl-2-nitrobenzoate[34] (392 mg, 2.00 mmol), dibenzoyl peroxide (24 mg, 0.10 mmol), and *N*-bromosuccinimide (374 mg, 2.10 mmol) in carbon tetrachloride (4 mL) was heated (90 °C, 23.5 h) and irradiated as described above. Solvent removal followed by chromatography (hexanes−EtOAc, 19:1) gave methyl 3-bromomethyl-2-nitrobenzoate (300 mg, 1.09 mmol, 55%) as faint yellow crystals:[35] mp 90−90.5 °C; ^{1}H NMR δ 7.95 (d, J = 7.7 Hz, 1H), 7.73 (d, J = 7.7 Hz, 1H), 7.57 (t, J = 7.6 Hz, 1H), 4.44 (s, 2H), 3.89 (s, 3H); ^{13}C NMR δ 163.5 (+), 149.3 (+), 135.3 (−), 131.2 (−), 130.8 (−), 130.3 (+), 124.3 (+), 53.2 (−), 25.5 (+); IR (neat) 1727, 1535, 1289 cm^{-1}. Anal. Calcd for $C_9H_8BrNO_4$: C, 39.44; H, 2.94. Found: C, 39.53; H, 2.97.

Triphenylphosphine (1.28 g, 4.86 mmol) was added to a solution of methyl 3-bromomethyl-2-nitrobenzoate (1.24 g, 4.53 mmol) in chloroform (20 mL). The solution was heated at reflux (15 min). After cooling to ambient temperature, dry diethyl ether (150 mL) was added to precipitate the Wittig salt. The slurry was filtered to give a white powder. The powder was washed with dry diethyl ether (100 mL) and dried under high-vacuum to give the crude phosphonium salt (1.96 g, 3.65

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(33) The reaction was followed by ^{1}H NMR.
(34) Somei, M.; Saida, Y.; Komura, N. *Chem. Pharm. Bull.* **1986**, *34*, 4116.
(35) Fractions containing an unseparable mixture of starting material and dibrominated product were also isolated.

mmol, 75%). The salt was used as such without further purification.

Methanal (g) was bubbled through a purple solution of the salt (1.96 g, 3.66 mmol) and triethylamine (2.73 mL, 19.6 mmol) in dichloromethane (70 mL) at ambient temperature. The purple color was discharged within 5 min of addition of the methanal. The solvent was removed to afford a yellowish-white crystalline residue. The solvent was removed from the filtrate to give the crude product. Chromatography using hexanes−EtOAc (8:2) as eluent gave **18** (761 mg, 3.67 mmol, 100%) as pale yellow crystals.

5-Bromo-2-nitrophenyl Trifluoromethanesulfonate. To a solution of 5-bromo-2-nitrophenol[31] (5.77 g, 26.5 mmol) in pyridine (25 mL), cooled in an ice-bath, was added trifluoromethanesulfonic acid anhydride (4.79 mL, 28.5 mmol) under an argon atmosphere. The resulting orange reaction mixture was stirred for 1 h, removed from the ice bath, and stirred an additional 20.5 h at ambient temperature. H_2O (50 mL) was added, and the mixture was extracted with CH_2Cl_2 (4 × 50 mL). The combined organic phases were washed with H_2O (4 × 30 mL), dried ($MgSO_4$), filtered, and evaporated to afford a brown oil. The crude product was purified by chromatography (hexanes−EtOAc, 8:2) to give 5-bromo-2-nitrophenyl trifluoromethanesulfonate (5.89 g, 16.8 mmol, 63%) as a pale yellow oil: ^{1}H NMR δ 8.12 (d, J = 8.7 Hz, 1H), 7.80 (d, J = 8.7 Hz, 1H), 7.66 (s, 1H); ^{13}C NMR δ 141.5 (−), 140.4 (−), 132.7 (+), 129.4 (−), 127.8 (+), 127.5 (+), 118.5 (q, J = 1274 Hz, −); IR (neat) 1593, 1537, 1434, 1347, 1215 cm^{-1}. Anal. Calcd for $C_7H_3NO_5S$: C, 24.02; H, 0.86. Found: C, 24.10; H, 0.94.

4-Bromo-2-ethenylnitrobenzene (19).[36] To a solution of 5-bromo-2-nitrophenyl trifluoromethanesulfonate (3.51 g, 10.0 mmol) and vinyltri-*n*-butyltin (2.93 mL, 11.0 mmol) in dioxane (40 mL) was added, under a positive flow of nitrogen, bis(dibenzylideneacetone)palladium(0) (288 mg, 0.50 mmol), triphenylphosphine (525 mg, 2.00 mmol), and LiCl (1.48 g, 30.0 mmol), together with a few crystals of 2,6-(1,1-dimethylethyl)-phenol. The solution was heated at reflux (15.5 h), whereupon a yellow-red solution containing a black precipitate was formed. The reaction mixture was cooled to ambient temperature, and the solvent was removed to give a black oil. The oil was dissolved in dichloromethane (20 mL), washed with NH_4OH (10%, aq, 3 × 20 mL) and H_2O (3 × 20 mL), and dried ($MgSO_4$). Removal of the solvent gave a two-phase residue consisting of a black oil (bottom) and a yellow oil (top), which was purified by two consecutive chromatographies using for the first column hexanes−EtOAc (19:1) as eluent and for the second column hexanes−EtOAc (49:1) to give **19** (1.85 g, 8.13 mmol, 81%) as yellow crystals.

2-Ethenyl-1,3-dinitrobenzene (20). Bromine (1.23 mL, 24.0 mmol) was added, over a 2 min period, to a boiling solution of 2-methyl-1,3-dinitrobenzene (1.82 g, 10.0 mmol) and benzoyl peroxide (242 mg, 1.00 mmol) in carbon tetrachloride (20 mL) under irradiation using a 100 W lamp. Under constant heating and irradiation, the mixture was monitored by TLC, and small increments of benzoyl peroxide and bromine were added until all starting material was consumed. When completed, the solution was allowed to cool to ambient temperature followed by solvent removal. The crude product was purified by chromatography (hexanes-EtOAc, 9:1) to give 2-bromomethyl-1,3-dinitrobenzene (2.07 g, 7.92 mmol, 79%) as white crystals: mp 73−74 °C; ^{1}H NMR δ 8.10 (d, J = 8.1 Hz, 2H), 7.68 (t, J = 8.2 Hz, 1H), 4.94 (s, 2H); ^{13}C NMR δ 149.9 (+), 130.2 (−), 128.6 (−), 126.5 (+), 20.3 (+); IR (neat) 1530, 1355 cm^{-1}. Anal. Calcd for $C_7H_5BrN_2O_4$: C, 32.21; H, 1.93. Found: C, 32.46; H, 2.02.

Triphenylphosphine (2.02 g, 7.70 mmol) was reacted with 2-bromomethyl-1,3-dinitrobenzene (1.83 g, 7.00 mmol) in chloroform (30 mL), as described above, to give a crude phosphonium salt (3.71 g, 6.90 mmol, ≤90%) as a bright yellow powder. The salt was used as such without further purification. Spectral data of the crude product: ^{1}H NMR δ 8.13 (d, J = 8.1 Hz, 2H), 7.91−7.57 (m, 16H), 5.77 (d, J = 14.2 Hz, 2H).

A solution of the salt (1.00 g, 1.88 mmol) in dichloromethane (50 mL) was reacted with triethylamine (514 μL, 4.00 mmol) and methanal (g) as described above. Removal of solvent and purification by chromatography (hexanes−EtOAc, 9:1 followed by hexanes−EtOAc, 8:2) gave **20** (354 mg, 1.71 mmol, 91%) as pale yellow crystals: mp 82−83 °C; ^{1}H NMR δ 8.05 (d, J = 8.1 Hz, 2H), 7.61 (t, J = 8.1 Hz, 1H), 7.04 (dd, J = 17.8 and 11.5 Hz, 1H), 5.53 (d, J = 11.5 Hz, 1H), 5.34 (d, J = 17.8 Hz, 1H); ^{13}C NMR δ 150.1 (+), 128.8 (−), 128.6 (+), 128.0 (−), 127.2 (−), 121.3 (+); IR (neat), 1532, 1361 cm^{-1}. Anal. Calcd for $C_8H_6N_2O_4$: C, 49.49; H, 3.12. Found: C, 49.57; H, 3.16.

Indole (21).[37] To an oven-dried, threaded ACE glass pressure tube was added 2-nitrostyrene (**4**)[38] (298 mg, 2.00 mmol), palladium diacetate (26 mg, 0.12 mmol), triphenylphosphine (124 mg, 0.48 mmol), and 4 mL of MeCN. The tube was fitted with a pressure head, the solution was saturated with CO (four cycles to 4 atm of CO), and the reaction mixture was heated to 70 °C (oil bath temperature) under CO (4 atm) until all starting material was consumed (15 h) as judged by TLC. The reaction mixture was diluted with HCl (aq, 10%, 10 mL) and extracted with Et_2O (3 × 10 mL). The combined organic phases were washed with HCl (aq, 10%, 10 mL) and dried ($MgSO_4$), and the solvent was removed to give the crude product. The crude product was purified by chromatography (hexanes−EtOAc, 9:1) to give **21** (203 mg, 1.75 mmol, 87%) as white crystals.

2-Methylindole (22).[39] A solution of 2-(1-propenyl)nitrobenzene (5)[10] (326 mg, 2.00 mmol), $Pd(OAc)_2$ (26 mg, 0.12 mmol), and PPh_3 (124 mg, 0.48 mmol) in MeCN (4 mL) was heated (24 h) under CO (4 atm) as described above. Extraction and chromatography (hexanes−EtOAc, 9:1) gave **22** (274 mg, 1.92 mmol, 96%) as faint yellow crystals.

2,3-Dimethylindole (23).[40] A solution of **6**[41] (161 mg, 0.91 mmol), $Pd(OAc)_2$ (12 mg, 0.05 mmol), and PPh_3 (57 mg, 0.22 mmol) in MeCN (2 mL) was heated (21.5 h) under CO (4 atm) as described above. Extraction and chromatography (hexanes−EtOAc, 9:1) gave **23** (128 mg, 0.88 mmol, 97%) as white crystals.

2-Phenylindole (24).[42] A solution of *trans*-**7**[9b] (182 mg, 0.81 mmol), $Pd(OAc)_2$ (11 mg, 0.05 mmol), and PPh_3 (52 mg, 0.20 mmol) in MeCN (4 mL) was heated (18.5 h) under CO (4 atm) as described above. Extraction and chromatography (hexanes−EtOAc, 9:1) gave **24** (156 mg, 0.81 mmol, 100%) as white crystals.

Similar reaction of a 1:1 mixture of *cis*- and *trans*-**7** (225 mg, 1.00 mmol), $Pd(OAc)_2$ (13 mg, 0.06 mmol), and PPh_3 (63 mg, 0.24 mmol) in MeCN (4 mL) was heaed (21 h) under CO (4 atm) gave **24** (176 mg, 0.91 mmol, 91%).

5-Methylindole (25).[43] A solution of **8** (152 mg, 0.93 mmol), $Pd(OAc)_2$ (13 mg, 0.06 mmol), and PPh_3 (62 mg, 0.24 mmol) in MeCN (4 mL) was heated (48 h) under CO (4 atm) as described above. Additional $Pd(OAc)_2$ (6 mg, 0.03 mmol) and PPh_3 (8 mg, 0.03 mmol) were added, and the mixture was pressurized and heated (24 h). Extraction and chromatography (hexanes−EtOAc, 9:1) gave **25** (62 mg, 0.47 mmol, 51%) as faint yellow crystals.

4-Methoxyindole (26).[44] A solution of **9** (179 mg, 1.00 mmol), $Pd(OAc)_2$ (13 mg, 0.06 mmol), and PPh_3 (62 mg, 0.24 mmol) in MeCN (2 mL) was heated (20 h) under CO (4 atm) as described above. Extraction and chromatography (hexanes−EtOAc, 9:1) gave **26** (131 mg, 0.89 mmol, 89%) as faint yellow crystals.

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(43) Aldrich Library of Spectra: ^{1}H and ^{13}C NMR spectra **3**,122 C, FT-IR spectra **2**,654 B.

(44) Aldrich Library of Spectra: ^{1}H and ^{13}C NMR spectra **3**,127 C, FT-IR spectra **2**,657 C.

5-Methoxyindole (27).[8] A solution of **10** (358 mg, 2.00 mmol), $Pd(OAc)_2$ (26 mg, 0.12 mmol), and PPh_3 (124 mg, 0.48 mmol) in MeCN (4 mL) was heated (19 h) under CO (4 atm) as described above. Extraction and chromatography (hexanes−EtOAc, 9:1) gave **27** (185 mg, 1.26 mmol, 63%) as faint yellow crystals.

6-Methoxyindole (28).[8] A solution of **11** (358 mg, 2.00 mmol), $Pd(OAc)_2$ (26 mg, 0.12 mmol), and PPh_3 (124 mg, 0.48 mmol) in MeCN (4 mL) was heated (21 h) under CO (4 atm) as described above. Extraction and chromatography (hexanes: EtOAc, 9:1) gave **28** (116 mg, 0.79 mmol, 40%) as faint yellow crystals.

6-Methoxy-3-methylindole (29).[45] A solution of **12** (386 mg, 2.00 mmol), $Pd(OAc)_2$ (26 mg, 0.12 mmol), and PPh_3 (124 mg 0.48 mmol) in MeCN (4 mL) was heated (24 h) under CO (4 atm) as described above. Extraction and chromatography (hexanes−EtOAc, 19:1) gave **29** (261 mg, 1.62 mmol, 81%) as white crystals.

4-Hydroxyindole (30).[46] A solution of **13** (207 mg, 1.25 mmol), $Pd(OAc)_2$ (18 mg, 0.08 mmol), and PPh_3 (84 mg, 0.32 mmol) in MeCN (4 mL) was heated overnight under CO (4 atm) as described above. Extraction and chromatography (hexanes:EtOAc, 7:3) gave **30** (159 mg, 1.20 mmol, 96%) as faint yellow-brown crystals.

4-[(Trifluoromethyl)sulfonyl]indole (31). A solution of 2-ethenyl-3-nitrophenyl trifluoromethanesulfonate (**14**)[24] (594 mg, 2.00 mmol), $Pd(OAc)_2$ (26 mg, 0.12 mmol), and PPh_3 (124 mg, 0.48 mmol) in MeCN (4 mL) was heated (48 h) under CO (4 atm) as described above. Extraction and chromatography using hexanes−EtOAc (9:1) followed by hexanes−EtOAc (8: 2) gave 2-ethenyl-3-nitrophenyl trifluoromethanesulfonate (230 mg, 0.77 mmol, 39%) followed by **31** (210 mg, 0.79 mmol, 40%), the latter as a faint yellow oil: ^{1}H NMR δ 8.39 (br s, 1H), 7.33 (d, J = 7.9 Hz, 1H), 7.21−7.15 (m, 2H), 7.10 (d, J = 7.9 Hz, 1H), 6.68 (s, 1H); ^{13}C NMR δ 142.2 (+), 138.0 (+), 125.9 (−), 121.8 (−), 120.9 (+), 118.8 (q, J = 318 Hz, +), 111.7 (−), 111.5 (−), 98.7 (−); IR (neat) 3447, 1414, 1210 cm^{-1}. Anal. Calcd for $C_9H_6F_3NO_3$: C, 40.76; H, 2.28. Found: C, 40.68; H, 2.35.

Methyl Indole-4-carboxylate (32).[47] A solution of **15** (414 mg, 2.00 mmol), $Pd(OAc)_2$ (26 mg, 0.12 mmol), and PPh_3 (124 mg, 0.48 mmol) in MeCN (4 mL) was heated (23 h) under CO (4 atm) as described above. Extraction and chromatography (hexanes−EtOAc, 9:1) gave **32** (350 mg, 2.00 mmol, 100%) as faint yellow crystals.

Methyl Indole-5-carboxylate (33).[8] A solution of **16** (414 mg, 2.00 mmol), $Pd(OAc)_2$ (26 mg, 0.12 mmol), and PPh_3 (124 mg, 0.48 mmol) in MeCN (4 mL) was heated (120 h) under CO (4 atm) as described above. Extraction and chromatography (hexanes:EtOAc, 9:1) gave methyl 3-ethenyl-4-nitrobenzoate (180 mg, 0.87 mmol, 43%) followed by **33** (165 mg, 0.94 mmol, 47%), the latter as faint yellow crystals.

Methyl Indole-6-carboxylate (34).[8] A solution of **17** (414 mg, 2.00 mmol), $Pd(OAc)_2$ (26 mg, 0.12 mmol), and PPh_3 (124 mg, 0.48 mmol) in MeCN (4 mL) was heated (21 h) under CO (4 atm) as described above. After this time, some starting material remained (by TLC) and an additional amount of $Pd(OAc)_2$ (26 mg, 0.12 mmol) and PPh_3 (124 mg, 0.48 mmol) was added. The mixture was heated for another 25 h to give, after extraction and chromatography (hexanes:EtOAc, 9:1), **34** (274 mg, 1.57 mmol, 78%) as faint yellow crystals.

Methyl Indole-7-carboxylate (35).[8] A solution of **18** (414 mg, 2.00 mmol), $Pd(OAc)_2$ (26 mg, 0.12 mmol), and PPh_3 (124 mg, 0.48 mmol) in MeCN (4 mL) was heated (27 h) under CO (4 atm) as described above. After this time, some starting material remained (by TLC), and additional $Pd(OAc)_2$ (26 mg, 0.12 mmol) and PPh_3 (124 mg, 0.48 mmol) were added. The mixture was heated for another 48 h, affording, after extraction and chromatography (hexanes−EtOAc, 9:1), **35** (260 mg, 1.40 mmol, 71%) as faint yellow crystals and 6-carbomethoxy-2-ethenylnitrobenzene (110 mg, 0.53 mmol, 27%).

4-Bromoindole (2).[19] A solution of 3-bromo-2-ethenylnitrobenzene (**1**)[20] (456 mg, 2.00 mmol), $Pd(OAc)_2$ (26 mg, 0.12 mmol), and PPh_3 (124 mg, 0.48 mmol) in MeCN (4 mL) was heated (15 h) under CO (4 atm) as described above. Extraction and chromatography (hexanes:EtOAc, 19:1) gave **2** (328 mg, 1.67 mmol, 84%) as faint yellow crystals.

4-Bromoindole (2) and Methyl *N*-(3-Bromo-2-ethenylphenyl)carbamate (3). A solution of 3-bromo-2-ethenylnitrobenzene (**1**) (456 mg, 2.00 mmol), $Pd(OAc)_2$ (26 mg, 0.12 mmol), and dppp (50 mg, 0.12 mmol) in DMF (4 mL) and MeOH (2 mL) was heated (22 h) under CO (4 atm) as described above. Extraction and chromatography (hexanes:EtOAc, 19:1) gave, in order of elution, **3** (88 mg, 0.34 mmol, 17%) as white crystals followed by **2** (297 mg, 1.52 mmol, 76%) as faint yellow crystals. Analytical data for **3**: mp 94−95 °C; ^{1}H NMR δ 8.08 (d, J = 7.9 Hz, 1H), 7.35 (s, 1H), 7.28 (d, 8.1 Hz, 1H), 7.12 (t, J = 8.2 Hz, 1H), 6.60 (dd, J = 18.0 and 11.4 Hz, 1H), 5.73 (dd, J = 11.3 and 1.2 Hz, 1H), 5.48 (dd, J = 18.3 and 1.5 Hz, 1H), 3.76 (s, 3H); ^{13}C NMR δ 153.7 (+), 136.3 (+), 133.4 (−), 129.0 (−), 128.2 (−), 126.9 (−), 123.3 (+), 122.3 (+), 118.0 (−), 52.4 (+); IR (neat) 3278, 1718, 1692 cm^{-1}. Anal. Calcd for $C_{10}H_{10}BrNO_2$: C, 46.90; H, 3.94. Found: C, 46.64; H, 4.05.

4-Nitroindole (37).[48] A solution of **20** (388 mg, 2.00 mmol), $Pd(OAc)_2$ (26 mg, 0.12 mmol), and PPh_3 (124 mg, 0.48 mmol) in MeCN (4 mL) was heated overnight (26 h) under CO (4 atm) as described above. Extraction and chromatography (hexanes−EtOAc, 9:1) gave **37** (310 mg, 1.78 mmol, 89%) as fine yellow crystals.

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