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Synthesis of Indoles by Reductive Cyclization of Nitro Compounds Using Formate Esters as CO Surrogates

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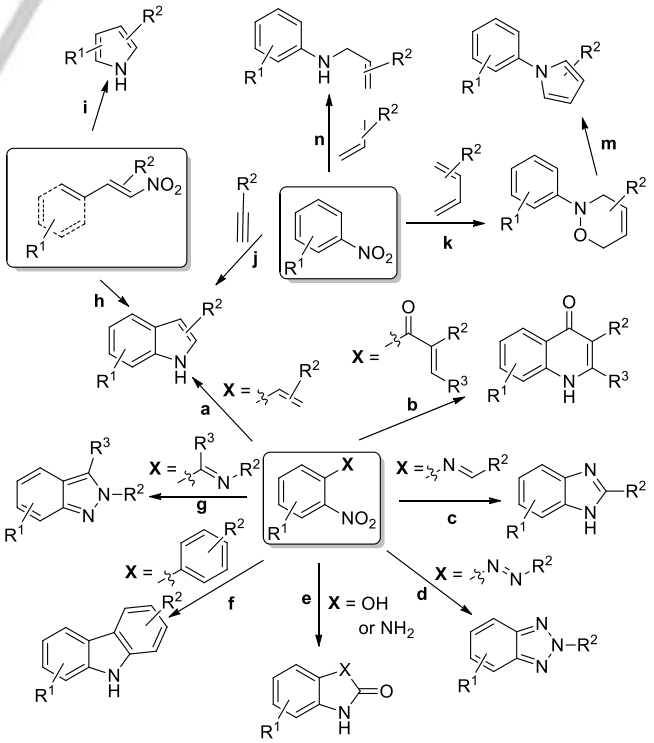
Abstract: Alkyl and aryl formate esters were evaluated as CO sources in the Pd- and Pd/Ru-catalyzed reductive cyclization of 2-nitrostyrenes to give indoles. Whereas the use of alkyl formates requires the presence of a ruthenium catalyst such as $Ru_3(CO)_{12}$, the reaction with phenyl formate can be performed by using a Pd/phenanthroline complex alone. Phenyl formate was found to be the most effective CO source and the desired products were obtained in excellent yields, often higher than those previously reported by the use of pressurized CO. The reaction tolerates many functional groups, including sensitive ones like a free aldehydic group or a pendant pyrrole. Detailed experiments and kinetic studies allow to conclude that the activation of phenyl formate is base-catalyzed and that the metal play no role in the decarbonylation step. The reactions can be performed in a single thick-walled glass tube with as little as 0.2 mol-% palladium catalyst and even on a 2 g scale. The same protocol can be extended to other nitro compounds, affording different heterocycles.

Introduction

The catalytic reductive carbonylation of aromatic nitro compounds is an efficient method for the preparation of a large variety of bulk[1] and fine[2] chemicals. Specifically, many nitrogen containing heterocycles have been previously synthesized from suitably *ortho*-substituted nitroarenes using CO as a stoichiometric reductant and examples of *inter*-molecular reactions and of reactions employing nitroalkenes as reagents are also known (Scheme 1).[3] Despite of the high efficiency of many of these reactions, they have not become of widespread use. The most likely reason for this is that they involve the use of pressurized CO, requiring safety measures that are not available in most synthetic organic laboratories. This problem is shared with other transformations employing gaseous CO. Indeed, despite the fact that most of the largest scale homogeneously catalyzed industrial processes are carbonylation reactions, the use of the same reactions at the laboratory scale is much less common. To allow standard organic synthesis laboratories to employ carbonylation reactions, a number of solid or liquid molecules able to liberate CO *in situ* have been developed, especially in the last decade.[4] These allow performing the reactions in thick-walled borosilicate glass vessels (also called pressure tubes), thus avoiding the need for high-pressure equipment and CO lines.

We started searching for a suitable CO surrogate to perform nitroarene reductive cyclization reactions many years ago and selected formate esters because of their commercial availability, low cost and low toxicity. We also chose to investigate the Pd-catalyzed synthesis of indoles from *o*-nitrostyrenes (Scheme 1, path **a**) as the first reaction to test and decided to operate in a single glass pressure tube because this equipment is cheap and available in different sizes. A steel autoclave can also be employed, but without using pressurized CO. Note that some of other known CO-releasing reagents require the use of two-chamber reactors to separate the CO-releasing reaction from the carbonylation one, a less convenient and versatile apparatus. When we started this study, no alternative had been reported to the use of gaseous CO in nitroarene cyclization reactions. More recently, the use of $Mo(CO)_6$ was reported to this aim.[5] However, this CO source is highly toxic and is not suitable for large scale applications. Very recently, Wu also employed aryl formates to carbonylate nitroarenes.[6]



Scheme 1. Selected transition-metal catalyzed syntheses of N-heterocycles from nitro compounds using CO as the reductant.

In this paper, we report a full account of our studies on the use of formate esters in the synthesis of indoles from 2-nitrostyrenes. A preliminary account of some of the results here reported has been previously published.[7]

Results and Discussion

Use of alkyl formates

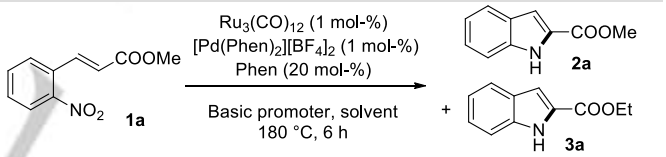
Owing to their very low cost, our initial investigation was devoted to prove if alkyl formates could be successful CO surrogates in the reductive cyclization of methyl (*E*)-2-nitrocinnamate (**1a**). Among formate esters, methyl formate is not only the cheapest, but also the one that has been more extensively investigated. It has long been known that its decomposition into CO and methanol can be promoted by strong bases, but the latter would not be compatible with most catalytic processes. On the other hand, $Ru_3(CO)_{12}$ has also been found to be an active catalyst for this decomposition[8] and this complex is surely compatible with the present reaction because it has long been known to catalyze reductive carbonylation and cyclization reactions of nitroarenes, including the synthesis of indoles.[9] The activity of $Ru_3(CO)_{12}$ for the decarbonylation of methyl formate is best promoted by phosphine ligands, but the latter are not compatible with a stable catalytic system for nitroarene reductive carbonylation because they react directly with the substrate to give phosphine oxides under typical reaction conditions.[10] Fortunately, 1,10-phenanthroline (Phen) was also reported to be effective as a $Ru_3(CO)_{12}$ activator.[11] Besides this, Phen and its substituted derivatives are also the ligands of choice to stabilize palladium to give the most active to date catalytic systems for a number of carbonylation and reductive carbonylation reactions of nitroarenes.[3d, 3o, 3q, 3u, 12] Moreover, the combination of a palladium complex, $Ru_3(CO)_{12}$ and phenanthroline has also been already tested and the two metals found to cooperate rather than to inhibit each other.[11, 13]

With this knowledge in mind, we started investigating the decomposition of methyl formate in the presence of $Ru_3(CO)_{12}$ and Phen in an autoclave. However, it turned out that in order to decompose methyl formate at a convenient rate, the reaction has to be performed at 180 °C and at this temperature methyl formate (b.p. 36 °C) generates by itself a vapor pressure of about 11 bar. The latter is at the limits of what can be withstood by glass pressure tubes, making their use unsafe. We thus moved to *n*-butyl formate (b.p. 107 °C) as a viable alternative.

Results are summarized in Table 1. The reaction conducted with palladium alone only gave a small conversion of the starting nitrostyrene (entry 1). In contrast, the use of $Ru_3(CO)_{12}$ alone was found to be effective A fair selectivity in indole was achieved, but only a moderate conversion of the nitrostyrene was observed (entry 2). The combination of the two metals allowed for an increased yield (entry 3). Organic bases accelerate the reaction (compare entry 4 with entries 3, 6-8), but only in the presence of Et_3N was an increase in selectivity towards the desired indoles **2a** observed (entry 3). Note that the addition of the weak base Et_3N to the reaction mixture has been shown to be beneficial for most, although not all, reductive cyclization reactions of nitroarenes by CO.[2d] However, in the present case, when Et_3N was used, ethyl 1*H*-indole-2-carboxylate (**3a**), was also produced. Increasing the reaction time allowed for a higher conversion and an increased selectivity in both indoles **2a** and **3a**. Under the same reaction conditions, benzyl and methyl formate gave similar results (entries 9 and 10, respectively). A few attempts were also made to use solvent mixtures in which only 1 mL of *n*-butyl formate was employed with 9 mL of another solvent (DMF, CH_3CN, toluene. Entries 11-13), but in all cases conversion and selectivity in indole decreased.

The formation of **3a** when Et_3N is employed as base was not expected. Small amounts of the ethyl ester of the starting nitrostyrene were also observed. It is known that some mononuclear ruthenium complexes catalyze the decomposition of Et_3N to afford, among others, ethanol[14] and the latter may be involved in a transesterification reaction. However, this is unlikely to be the correct explanation because larger amounts of *n*-butanol are surely formed as the reaction proceeds and no or at most trace amounts of the butyl ester of 1*H*-indole-2-carboxylic acid could be detected by GC-MS among the reaction products. On the other hand, it has also been reported that $Ru_3(CO)_{12}$ catalyzes the exchange of alkyl groups among Et_3N and a different tertiary amine.[15] The reaction proceeds by the formation of different trinuclear cluster species. Although, to the best of our knowledge, it has not been reported that esters can play the role of the second amine, the formation of **3a** can be easily rationalized if we suppose that the same kind of intermediates that are able to break and reform C-N bonds are also able to do the same with C-O bonds. Note that even several palladium complexes are able to activate the C-N bond of

Table 1. [Pd]/[Ru]-catalyzed reductive cyclization of **1a** using *n*-butyl formate as CO source: influence of various reaction parameters.

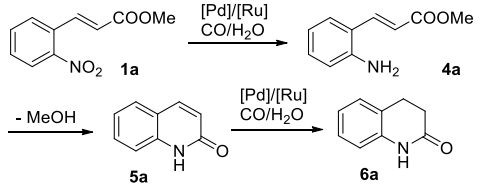


Entry	Solvent	Basic promoter	1a Conv. [%][b]	2a Select. [%][c]	3a Select. [%][c]	2a+3a Select. [%][c]
1[d]	*n*-Butyl formate	Et_3N	15	traces	-	<1
2[e]	*n*-Butyl formate	Et_3N	72	45	2	47
3	*n*-Butyl formate	Et_3N	85	40	8	48
4	*n*-Butyl formate	-	53	23	-	23
5[f]	*n*-Butyl formate	Et_3N	96	65	21	86
6	*n*-Butyl formate	DBU[g]	>99	29	-	29
7	*n*-Butyl formate	DABCO[h]	97	24	-	24
8	*n*-Butyl formate	DIPEA[i]	71	24	-	24
9	Methyl formate[j]	Et_3N	48	52	traces	52
10	Benzyl formate	Et_3N	>99	53	-	53
11[k]	*n*-Butyl formate/CH_3CN	Et_3N	53	18	5	23
12[k]	*n*-Butyl formate/DMF	Et_3N	70	40	<1	40
13[k]	*n*-Butyl formate/Toluene	Et_3N	28	21	traces	21

[a] Reaction conditions: **1a** = 0.27 mmol, mol ratio $[Pd(Phen)_2][BF_4]_2$: $Ru_3(CO)_{12}$: Phen : **1a** = 1:1:20:100, mol ratio basic promoter: **1a** = 2 : 1, solvent (10 mL), at 180 °C for 6 hours in a sealed pressure tube. Results based on GC analysis using biphenyl as the internal standard. [b] With respect to starting **1a**. [c] With respect to converted **1a**. [d] Only $[Pd(Phen)_2][BF_4]_2$ was used. [e] Only $Ru_3(CO)_{12}$ was used; [f] Reaction time was 10 h; [g] 1,8-diazabicycloundec-7-ene. [h] 1,4-diazabicyclo[2.2.2]octane; [i] *N,N*-diisopropylethylamine. [j] The reaction was performed in a Teflon-coated 200 mL stainless steel autoclave. [k] 1 mL *n*-butyl formate and 9 mL of the other solvent.

tertiary amines, although, to the best of our knowledge, an exchange reaction such as that described for ruthenium has not been reported.[16]

The main side product was methyl 2-aminocinnamate (**4a**, Scheme 2). The latter was accompanied by its cyclization product, namely a lactam (**5a**). Traces of 3,4-dihydroquinolin-2(1*H*)-one (**6a**) were also detected by GC-MS, which can arise from the reduction of the conjugated C=C double bond in **5a**.



Scheme 2. Formation of byproducts during the reductive cyclization of **1a** into **2a** in the presence of *n*-butyl formate.

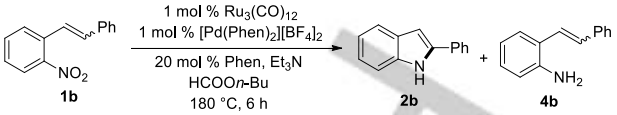
The formation of **4a** can be explained by a Ru-catalyzed reduction of nitro group. Indeed, it is known that $Ru_3(CO)_{12}$ in the presence of Phen[17] or even just Et_3N[18] is a very active catalyst for the reduction of nitroarenes to anilines by CO/H_2O. In fact, despite the use of distilled solvents and dried glassware, adventitious traces of water may be present both in the solvents and in the gaseous nitrogen. However, the over reduction of the nitro group might also be due to a ruthenium catalyzed transfer hydrogenation reaction in which butanol formed by formate decomposition act as the H-donor.

Using the reaction conditions previously employed in the case of methyl (*E*)-2-nitrocynnamate (**1a**), we extended the optimization study to 2-nitrostylbene (**1b**) for the synthesis of 2-phenylindole (**2b**) (Table 2). Since we obtained the starting material as a diasteroisomeric *E* and *Z* mixture, we examined the reactivity of both the pure diasteroisomers and their mixture. At variance with what observed with **1a**, in the current case the corresponding amine **4b** was detected as by-product to a much higher extent, which may simply be due to the fact that in this case it cannot evolve to other cyclic products (*vide supra*). As in the previous case, an elongation of the reaction time allowed for better conversions although a decrease in the selectivity in the desired indole **2b** was observed (Table 2, entry 2). Even in this case, bases other than Et_3N gave a less selective reaction (entries 3-5). It is worth noting that Et_3N is one of the most convenient organic bases both in terms of cost and easiness of removal from the reaction mixture, owing to its relatively low boiling point (89 °C).

A close look at the unreacted styrene in those cases in which the conversion was not complete evidenced that the starting material was much enriched into the *Z* isomer with respect to the initial 2:1 *Z*/*E* ratio. To better understand this point, the two isomers were separated and independently reacted. The outcome of the two separate reactions (Table 2, entries 6 and 7) evidences that the reaction is indeed slower in the case of the *Z* than in the case of *E* one. However, the selectivity followed an opposite trend. A similar effect has been previously observed in the case of the related cyclization of dimethylamino-substituted nitrostilbenes.[19]

Davies reported that the reactivity of a series 2-nitrostilbenes correlated with their reduction potential (more easily reducible

Table 2. [Pd]/[Ru]-catalyzed reductive cyclization of **1b** using *n*-butyl formate as CO source.



Entry	*Z*:*E* mol ratio	**1b** Conv. [%][b]	**2b** Select. [%][b]	**4b** Select. [%][b]
1	2:1	65	69	27
2[c]	2:1	>99	52	29
3[d]	2:1	>99	45	22
4[e]	2:1	>99	32	31
5[f]	2:1	41	23	32
6	Only *Z*	61	74	20
7	Only *E*	81	63	19

[a] Reaction conditions: 0.27 mmol **1b**, mol. ratio $[Pd(Phen)_2][BF_4]_2$:$Ru_3(CO)_{12}$:Phen:**1b** = 1:1:20:100; mol. ratio Et_3N:**1b** = 2:1; *n*-butyl formate 10 mL. Reactions were performed into heavy-wall glass tubes. [b] Conversion and selectivity were determined by GC analysis using biphenyl as the internal standard. [c] Reaction time was 10 h. [d] DBU was used instead Et_3N. [e] DABCO was used instead Et_3N. [f] DIPEA was used instead Et_3N.

nitrostyrenes react more quickly) and with the Hammet σ constant of the substituent on the nitroaryl ring when the same kind of cyclization reaction is performed with a Pd/Phen catalyst and under CO pressure.[3d] The activation of the nitroarene was consequently considered to be the r.d.s. of the reaction. This is in accord with the fact that the initial activation of nitroarenes by late-transition metal complexes has been shown to involve a single electron transfer from the metal to the nitroarene in all the cases in which it has been investigated.[20] The electronic effect of styryl group is expected to be essentially unvaried if in the *E* or *Z* configuration, but steric effects indirectly affect the reduction potential of the nitroarene. Indeed, it has long been known that *o*-nitrotoluene has a more negative reduction potential than *p*-nitrotoluene, despite electronic effects should be roughly the same.[21] The effect is due to the fact that the presence of an *ortho* substituent causes a tilting of the plane of the nitro group with respect to that of the phenyl ring and this tilting decreases the efficiency of the delocalization of the negative charge in the reduced species.

In order to check if the same effect of steric hindrance on the reduction potential operates in our case, a cyclic voltammetric study was performed. Only data for the *E* isomer have been previously reported in the literature.[22] As depicted in Figure 1, three cathodic peaks with peak potentials around -1.12 (**A**), -1.80 (**B**) and -2.30 V (**C**) were detected.

According to the literature, the first peak (**A** in Figure 1) is attributed to the quasi-reversible one-electron reduction of the nitro group to its radical anion.[22] At more negative potentials, the second peak (**B**) is attributed to the reversible one-electron reduction of the nitro radical-anion to the nitrodianion (Scheme 3). Finally, the third cathodic peak (**C**) at around -2.30 V arises from the irreversible reduction of the stilbene moiety. The involved species are depicted in Scheme 3 and the corresponding E_{pc} values are reported in Table 3.

Analyzing the available data as a whole, it is evident that the *Z* isomer is more difficult to reduce than the *E* one, in accord with our expectations. That ***Z*-2b** feels a strong steric repulsion is confirmed by its crystal structure clearly showing not only a twisting of the nitro group with respect to the aryl ring but even a

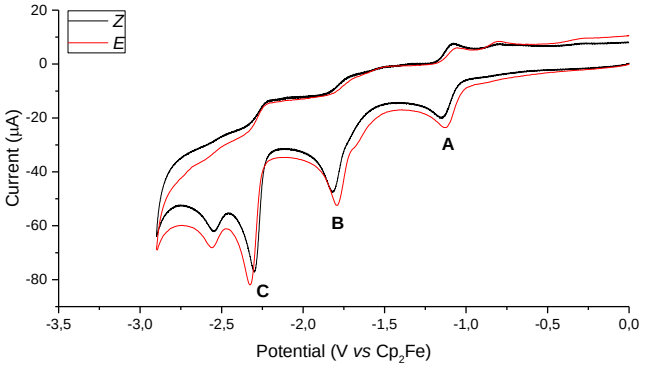
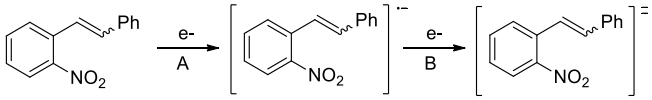


Figure 1. Cyclic voltammograms recorded of ***Z*-1b** and ***E*-1b**. The CV tests were conducted in anhydrous DMF with a substrate concentration of $6 \cdot 10^{-4}$ M + 0.1 M tetraethylammonium tetrafluoborate as supporting electrolyte, with a potential scan rate of 0.2 V·s-1.



Scheme 3. Electrochemical reduction steps of **1b.**

Table 3. Electrochemical data for reduction of **1b**.[a]

Peak	E_{pc} for *Z* isomer [V]	E_{pc} for *E* isomer [V]	ΔE_{pc} [mV]
A	-1.15	-1.12	30
B	-1.83	-1.81	20

[a] See footnote to Figure 1 for experimental conditions.

remarkable twisting of the two aryl moieties.[23] Unfortunately, no crystal structures of the *E* isomer has been reported in the literature. However, unsubstituted *trans*-stilbene shows a completely flat structure.[24]

It is also worth noting that at the end of the reaction employing either pure ***Z*-2b** or pure ***E*-2b**, a small amount of the other isomer was detected by GC. However, a control experiment in which pure ***Z*-2b** was reacted under the same experimental conditions (see caption to Table 2), but in the absence of any metal showed that 13% of the starting olefin had been converted into the *E* isomer. Thus, this effect may be ascribed to the high temperature employed only, without the necessity to claim for an effect of the catalysts. On the other hand, the byproduct **4b** was exclusively obtained as the *E* isomer even when pure ***Z*-2b** was used as reagent. This indicates that the catalytic system has the ability to isomerize the double bond and that the isomerization occurs more easily when the reduction of the nitro group proceeds.

The *n*-butyl formate protocol was applied to the synthesis of a few indoles (*vide infra* Table 9, conditions A), but isolated yields were lower than those achievable by the use of gaseous CO.

Use of phenyl formate

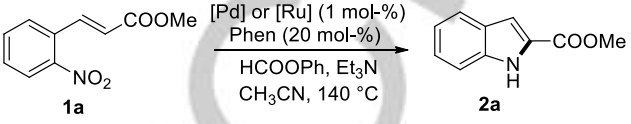
Since we started working in this field many years ago, the use of phenyl formate as a more effective CO surrogate than alkyl formates has been reported by several groups.[25] Gratifyingly, when phenyl formate was employed in a 1:9 mixture with CH_3CN, complete conversion and a moderate selectivity was achieved (Table 4, entry 1). Moreover, when the reaction temperature was lowered from 180 °C to 140 °C, the selectivity increased to 92% (entry 2). At lower temperatures, the selectivity decreased, although the conversion was still virtually complete. Thus, 140 °C was chosen for a further optimization.

In the first place, several Pd sources were tested (Table 4). In order to better differentiate the catalysts, both the reaction time and the formate amounts were halved.

All the tested palladium compounds were very effective in the transformation, leading to complete conversion. Significantly, an almost complete selectivity towards **2a** was observed with $Pd(CH_3CN)_2Cl_2$ (entry 6). In contrast to the *n*-butyl formate based protocol, the addition of $Ru_3(CO)_{12}$ is not necessary, but the presence of the ligand is still essential and poor results were obtained in its absence (values in parentheses in Table 4).

Note that by working at this temperature and in the absence of any ruthenium species, **3a** was not formed even though Et_3N

Table 4. Reductive cyclization of **1a** with HCOOPh: screening of Pd and Ru precatalysts.[a]



Entry	T [°C]	t [h]	Catalyst	**1a** Conv. [%][b],[c]	**2a** Select. [%][b],[c]
1[d]	180	6	$[Pd(Phen)_2][BF_4]_2$/ $Ru_3(CO)_{12}$	> 99	65
2[d]	140	6	$[Pd(Phen)_2][BF_4]_2$/ $Ru_3(CO)_{12}$	> 99	92
3[d]	120	6	$[Pd(Phen)_2][BF_4]_2$/ $Ru_3(CO)_{12}$	> 99	86
4[d]	90	6	$[Pd(Phen)_2][BF_4]_2$/ $Ru_3(CO)_{12}$	> 99	76
5	140	3	$[Pd(Phen)_2][BF_4]_2$	>99 (32)	94 (34)
6	140	3	$Pd(CH_3CN)_2Cl_2$	>99 (19)	98 (17)
7	140	3	$Pd(OAc)_2$	>99 (4)	92 (traces)
8	140	3	$Pd(dba)_2$	86 (4)	93 (traces)
9	140	3	$Ru_3(CO)_{12}$	23	79
10[e]	140	3	$Pd(CH_3CN)_2Cl_2$	58	95

[a] Reaction conditions: 0.27 mmol **1a**, 1 mol% of Pd catalyst and/or $Ru_3(CO)_{12}$, 20 mol% Phen, 500 μL of HCOOPh (corresponding to 17 equiv. with respect to **1a** or 8.5 fold the CO required by the reaction), 2 equiv. Et_3N (80 μL), in CH_3CN (10 mL). Reactions were performed into heavy-wall glass tubes. [b] Conversion and selectivity were determined by GC analysis using biphenyl as the internal standard. [c] Values in parentheses refer to the reactions performed omitting Phen. [d] Reaction performed in 1 mL HCOOPh + 9 mL CH_3CN. [e] Reaction performed in an autoclave under CO pressure (30 bar). No HCOOPh was added.

was still present. This supports the idea that a ruthenium species is responsible for the apparent transesterification reaction.

The identity of the best pre-catalyst, a chloride-containing complex, was somehow unexpected. It has long been known that when Pd/Phen complexes are employed as catalysts for the related carbonylation of nitroarenes to methyl arylcarbamates, non-coordinating anions must be used.[2c] Specifically, even if less than one equivalent of chloride with respect to palladium can have a promoting effect under certain conditions,[12b, 26] larger amounts strongly inhibit the catalytic activity.[12a] This is at least in part due to the very low solubility of $Pd(Phen)Cl_2$ in most solvents. Apparently, CH_3CN solubilizes the complex enough at the reaction temperature that the low solubility is no longer a problem.

Control experiments (Table S1, Supporting Information) show that removing any of the components of the catalytic system, palladium complex, phenyl formate, Et_3N, from the reaction mixture completely quench the catalytic activity.

Especially important is the comparison with the result obtained by working under CO pressure (in an autoclave) and in the absence of any formate (Table 4, entry 10). Both the selectivity and, more markedly, the conversion are lower for the reaction run under CO, showing that the use of a CO surrogate can be a first-choice strategy and not only a second option when an autoclave and a source of pressurized CO are not available.

While an autoclave is not necessary, a sealed vessel is still required. A reaction was performed in a standard Schlenk flask connected to a dinitrogen line. The temperature had to be lowered at the reflux temperature of the mixture (~82 °C). The reaction was very slow (Figure 2): after 9 h conversion was just 8%. However, when further 200 µL of HCOOPh were added, the reaction accelerated and a 19% conversion was reached. As a reference, performing the reaction at the same temperature into a pressure tube, 65% conversion and 97% selectivity were achieved after 9 h (Figure 2). These experiments prove that the low reactivity in an open vessel system is not due to a deactivation of the Pd catalysts but to a very low CO concentration in the liquid phase. They also show that pressure tubes are crucial to maximize the amount of CO in solution.

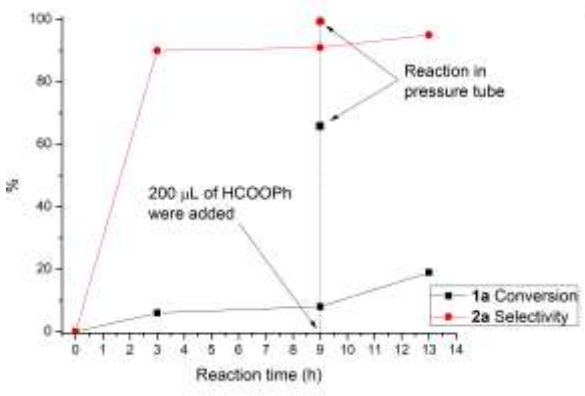


Figure 2. Reaction performed in a Schlenk flask under dinitrogen atmosphere and comparison reaction run in a sealed pressure tube. Reaction conditions: 0.27 mmol **1a,** 1 mol-% $Pd(CH_3CN)_2Cl_2$, 20 mol-% Phen, 1 equiv. Et_3N (40 µL), 500 µL of HCOOPh, in 10 mL CH_3CN. Reaction was conducted at reflux temperature (~82 °C). Conversion and selectivity were determined using GC (biphenyl as internal standard).

The amount of phenyl formate was optimized. As shown in Figure S1 (Supporting Information), the into a pressure tube formate amount can be lowered up to 3.4-fold the stoichiometric amount with respect to the required CO (2 equivalents of CO are needed) without altering the reaction outcome significantly. Further diminishing the HCOOPh amount led to a slight decrease of the selectivity, but to a drop in the conversion. The base amount was also optimized and just 1 equivalent of Et_3N (40 µL) is needed to achieve complete conversion and selectivity (Figure S2). Finally, the Phen amount could be lowered to 5 mol-% (Figure S3).

To handle suitable amounts of both starting materials and reaction products for a substrate scope study, the reaction was scaled-up by a factor of two. In order not to shift the coordination equilibria in the system, which are concentration-dependent: a) the catalyst and nitroarene amounts were doubled; b) the Phen, Et_3N and CH_3CN amounts were not changed; c) the amount of HCOOPh was such that its excess with respect to the stoichiometric amount required was unvaried. Under these conditions, complete conversion of **1a** and selectivity (GC analysis) into **2a** were achieved.

With the best conditions in our hands, the reaction scope was explored (*vide infra* Table 9, conditions B). A discussion of the obtained results is given later in this paper. Here it suffices to say that excellent results (isolated yield > 90%) were obtained in several cases and the reaction also gave good results with several more substrates. However, only moderate yields were obtained in the presence of sensitive groups such as an aldehyde or a pyrrole ring and a few substrates gave mixtures of products.

For this reason, we decided to make a further effort to optimize a new set of experimental conditions that could allow the reaction to be performed at a lower temperature, in the hope that this feature would have allowed to deal also with very reactive functional groups on the molecule. A further goal was to decrease the amount of catalyst in order to make the procedure more interesting even from an industrial point of view.

We initially tested the effect of lowering the catalyst amount when working at 120 °C (Table 5).

Table 5. Effect of catalyst loading in the $Pd(CH_3CN)_2Cl_2$ catalyzed reductive cyclization of **1a** using phenyl formate as a CO source.[a]

Entry	Catalyst loading [mol-%]	**1a** Conv. [%][b]	**2a** Select. [%][b]
1	1	98	>99
2	0.33	99	>99
3	0.2	99	98
4	0.1	97	87
5	0.02	27	21
6	0.01	3	48[c]

[a] Reaction conditions: 0.27 mmol **1a**, 5 mol-% Phen, 200 µL HCOOPh, 40 µL Et_3N, CH_3CN 10 mL, at 120 °C for 3 h. Reactions were performed into heavy-wall glass tubes. [b] Conversion and selectivity were determined by GC analysis using biphenyl as the internal standard. [c] Value affected by a large experimental error because of the low conversion value.

Gratifyingly, the catalyst amount can be decreased to 0.2 mol-% essentially without affecting the results (Table 5, entry 3) and the catalyst is active even at lower loadings, although with a decreased performance (Table 5, entries 4-6).

When we attempted to further lower the temperature to 100 °C we encountered a problem with the reproducibility of the reaction. Considering that this may have been due to an insufficient rate of CO generation (see also later), we tested the effect of increasing the amount of base (Table S2) and found that use of ~2.5 eq. of Et_3N with respect to the substrate (100 µL absolute amount) not only improved conversion and selectivity, but also solved the reproducibility problem.

The ligand identity plays a very important role in most catalytic systems and phenanthrolines substituted with electrondonating substituents affords better results than unsubstituted phenanthroline in several cases in the field of nitro compounds reduction by CO.[3p, 3u, 5b, 27] Moreover, the ligand-to-metal ratio is also very important and may vary between differently substituted phenanthrolines.[28] Thus, several experiments were run employing four different phenanthrolines. The most significant data from the point of view of evidencing the differences (the reaction time was lowered to 2 h to enhance them) are reported in Table 6. More data is reported in the Supporting Information (Tables S3 and S4).

Table 6. Effect of ligand identity in the $Pd(CH_3CN)_2Cl_2$ catalyzed reductive cyclization of **1a** using phenyl formate as CO source.[a]

Entry	Ligand	**1a** Conv. [%][b]	**2a** Select. [%][b]
1	Phenanthroline	84	97
2	4,7-Dimethoxyphenanthroline	76	97
3	3,4,7,8-Tetramethylphenanthroline	67	93
4	4,7-Dimethylphenanthroline	74	93

[a] Reaction conditions: 0.27 mmol **1a**, mol. 1 mol-% $Pd(CH_3CN)_2Cl_2$, 2.5 mol-% ligand; 200 µL HCOOPh, 100 µL Et_3N, CH_3CN 10 mL, at 100 °C for 2 h. Reactions were performed into heavy-wall glass tubes. [b] Conversion and selectivity were determined by GC analysis using biphenyl as the internal standard.

Over a range of ligand ratios and reaction times, phenanthroline was confirmed to be the best ligand.

Even the use of different phosphates as inorganic bases in place of Et_3N gave worse results (Table S5), but during attempts to better solubilize them in the reaction mixture by using DMF as a solvent or co-solvent we found an unexpected solvent effect (Table 7).

Table 7. Effect of DMF addition in the $Pd(CH_3CN)_2Cl_2$ catalyzed reductive cyclization of **1a** using phenyl formate as CO source.[a]

Entry	Volume DMF [mL]	**1a** Conv. [%][b]	**2a** Select. [%][b]
1	10	25	86
2	2	48	93
3	1	92	97
4	0.5	86	97
5	0.1	60	95
6	0	60	94
7[c]	1	15	92

[a] Reaction conditions: 0.27 mmol **1a**, 0.2 mol% $Pd(CH_3CN)_2Cl_2$, 5 mol% Phen, 200 µL HCOOPh, 100 µL of Et_3N, at 100 °C in CH_3CN + DMF (total volume 10 mL), for 2 h. Reactions were performed into heavy-wall glass tubes. Conversion and selectivity were determined using GC (biphenyl as the internal standard). [c] Na_3PO_4 was employed as a base in place of Et_3N.

Neat DMF is clearly inferior to neat CH_3CN as a reaction medium (Table 7, entries 1 and 6). However, lower amounts of DMF in CH_3CN can be highly beneficial on the reaction rate, with 1 mL DMF allowing an increase in conversion from 60% in neat CH_3CN to 92% in the 9:1 CH_3CN/DMF mixture. The selectivity in indole was less sensitive to the reaction medium, but the best result was again obtained at the 9:1 ratio. It may be noted that DMF was the ideal solvent under the reaction conditions reported by Davies for the same cyclization, but with gaseous CO.[3d]

Yet, such a large effect on conversion of just 10 % DMF was unexpected and will be worth to be investigated even in other reactions.

Further experiments were also run at 80 °C and 60 °C (Tables S6 and S7). A full conversion and virtually quantitative selectivity could still be obtained at 80 °C, but the catalyst loading had to be increased to 1 mol-% and 5 eq. of Et_3N were necessary to decompose phenyl formate at an acceptable rate. Thus, we decided not to develop these reaction conditions any further. However, working at less than 100 °C is clearly possible if this is advisable due to stability problems of the substrate or product.

One point that is virtually never analyzed in the literature on CO surrogates is the effect of the level of filling of the tube or flask employed to perform the reaction, which influence the headspace volume. As a matter of fact, neither for traditional reactions nor for reactions run in an autoclave, where the gaseous reagent is usually present in a large molar excess or is continuously refilled, this parameter is important. However, in the case of reactions in which CO is generated during the reaction, the headspace volume can have a very relevant role. Indeed, one must consider that, contrary to a reaction run under pressure, in which CO is initially present only in the gas phase and gradually dissolves in the liquid phase, here CO is generated directly in the liquid phase, but can then both escape into the gas phase and reenter the liquid phase from the latter. We have already shown above (Figure 2 and associated text) that if the reaction is run in a traditional Schlenk flask connected to a dinitrogen line, the reaction is much slower and stops well before the starting nitro compound is fully consumed. This observation evidences that some of the liberated CO can probably be intercepted by the palladium catalyst when still in the liquid phase, but under these conditions most of it escapes into the gas phase and is recaptured only to a small extent, if any. Likely, performing the same reaction in a closed vessel of large volume would produce a similar outcome. Overall, one must consider that different and competing effects arise when decreasing the solvent amount keeping all of the rest constant.

1) The decreasing of the solvent will result in a more concentrated solution and this should have a positive effect at least on the reaction rate.

2) The corresponding increasing of the headspace volume will result in a lower average CO pressure during the reaction and a less effective CO utilization. This may slow down the reaction and possibly also cause the deactivation of the catalyst or the onset of competing reactions that do not use CO (e.g. a Heck reaction in the present case when substrates containing aryl bromide moieties are employed).

3) Increasing the solvent amount should have the opposite effect, but much caution should be exerted in not leaving a too small headspace volume because this may cause the onset of a too high pressure and the explosion of the glass vessel. The

maximum amount of phenyl formate we employed was chosen so that even in the worst scenario, *i.e.* complete decomposition of the formate with no consumption of the produced CO, the pressure inside the tube would not exceed 10 bar even at the highest temperature.

Obviously, a strong dependency of the reaction outcome on the solvent and vessel volumes would detract from the general applicability of our protocol. Thus, we tested the effect of decreasing the solvent amount (Table 8)

Table 8. Effect of the solvent volume in the $Pd(CH_3CN)_2Cl_2$ catalyzed reductive cyclization of **1a** using phenyl formate as CO source.[a]

Entry	Volume CH_3CN [mL]	**1a** Conv. [%][b]	**2a** Select. [%][b]
1	10	60	94
2	5	67	96
3	2.5	67	90

[a] Reaction conditions: 0.27 mmol **1a**, 0.2 mol% $Pd(CH_3CN)_2Cl_2$, 5 mol% Phen, 200 µL HCOOPh, 100 µL of Et_3N, at 100 °C for 2 h. Reactions were performed into heavy-wall glass tubes. Conversion and selectivity were determined using GC (biphenyl as the internal standard).

Reducing the solvent from 10 to 5 and even 2.5 mL (resulting in an increase of the headspace from 13 to 18 and 20.5 mL respectively) had a small, whether not negligible, effect, showing that the optimized protocol tolerates quite large variations in the solvent and headspace volumes without compromising the outcome of the reaction.

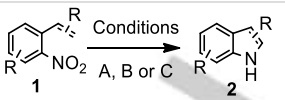
On the other hand, a strict exclusion of air while assembling the reactor (see Experimental for a description of the employed protocol) and use of dry solvents is essential to obtain good results. When a reaction was run under the conditions or entry 1 in Table 5, but assembling the reactor in the air, the conversion dropped from 98 to 10 %. Clearly, the catalytically active species is irreversibly destroyed by even low amounts of dioxygen. Conversely, the addition of 50 µL of water, in the absence of air, had little effect on the conversion, but the selectivity in indole dropped to 34% and larger amounts of **4a** were formed. Thus, use of dry solvents and strict exclusion of air are key points for obtaining good and reproducible results.

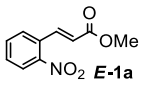
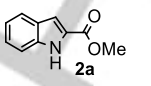
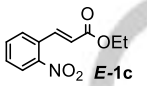
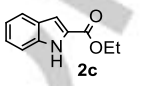
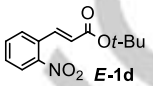
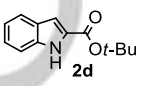
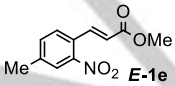
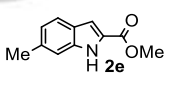
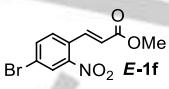
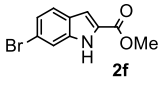
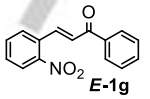
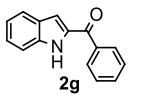
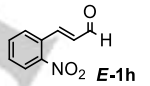
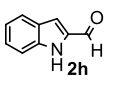
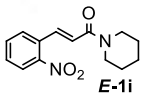
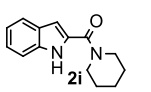
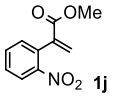
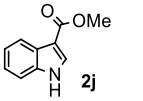
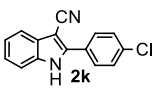
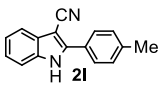
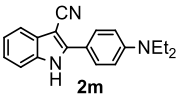
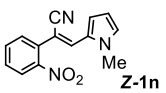
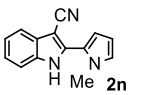
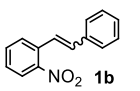
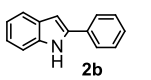
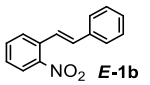
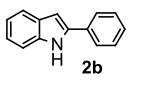
Substrate scope investigation

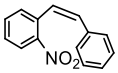
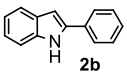
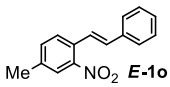
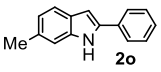
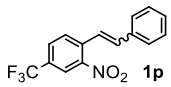
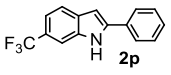
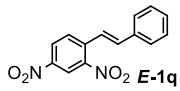
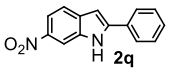
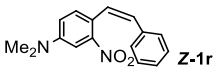
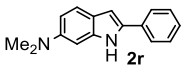
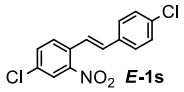
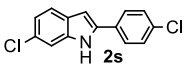
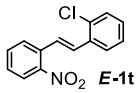
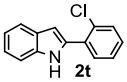
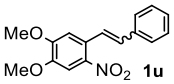
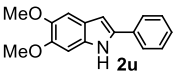
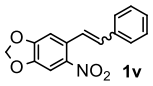
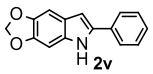
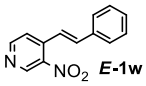
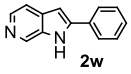
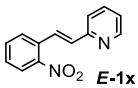
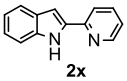
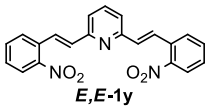
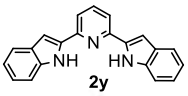
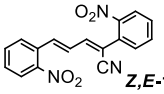
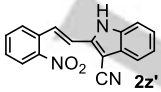
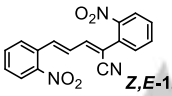
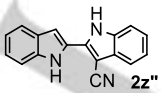
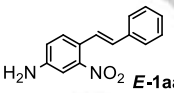
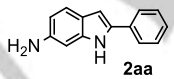
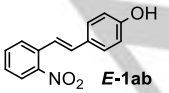
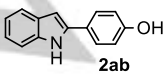
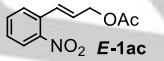
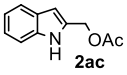
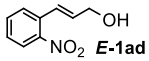
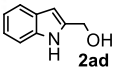
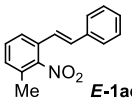
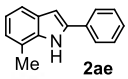
With this new set of optimized reaction conditions in our hands, we reinvestigated the substrate scope of the reaction, focusing on those substrates that either had not given high yields or had failed at all to give an isolable product under Conditions B. Several new substrates were also explored. To ensure that even less reactive substrates would give complete conversion under the same set of experimental conditions, a 1 mol-% catalyst loading was employed and the reaction time increased to 6 h. Results are shown in Table 9, Conditions C. Pure *E* or *Z* isomer of the starting nitrostyrenes or a mixture of the two was employed as a starting material depending on the synthetic procedure employed to prepare them.

A first glance to the results reported in the table immediately evidences that despite good results can be obtained in some cases under Conditions A, the obtained yields are always markedly lower than those achievable by the use of phenyl formate under both Conditions B and C. The results obtained under Conditions A will not be further discussed. As already

Table 9. Substrate scope under different experimental conditions.



Entry	Substrate	Product	Yield[a] A	B	C
1	 **E-1a**	 **2a**	62[b,c]	95 (99[b])	99[b]
2	 **E-1c**	 **2c**		92	
3	 **E-1d**	 **2d**		87	
4	 **E-1e**	 **2e**		96	
5	 **E-1f**	 **2f**		90[d]	
6	 **E-1g**	 **2g**		79[e]	
7	 **E-1h**	 **2h**		50[f]	65
8	 **E-1i**	 **2i**		73	91
9	 **1j**	 **2j**		45	64
10	 **Z-1k**	 **2k**		94	
11	 **Z-1l**	 **2l**		95[g]	
12	 **Z-1m**	 **2m**		95[g]	
13	 **Z-1n**	 **2n**		51	77
14	 **1b** *Z*:*E* = 2:1	 **2b**	52[b]	90[d]	
15	 **E-1b**	 **2b**			95[b]

16	 **Z-1b**	 **2b**			96[b]
17	 **E-1o**	 **2o**		71	96
18	 **1p**	 **2p**	37	98[g]	
19	 **E-1q**	 **2q**			78
20	 **Z-1r**	 **2r**		45[j]	60
21	 **E-1s**	 **2s**	70	92[h]	
22	 **E-1t**	 **2t**		69	94
23	 **1u**	 **2u**		-[k]	71
24	 **1v**	 **2v**		8[j]	72
25	 **E-1w**	 **2w**		91	
26	 **E-1x**	 **2x**	52	98	
27[l]	 **E,E-1y**	 **2y**		78	
28[l]	 **Z,E-1z**	 **2z'**			61
29[l]	 **Z,E-1z**	 **2z''**			90
30	 **E-1aa**	 **2aa**		-[k]	-[k]
31	 **E-1ab**	 **2ab**			-[k]
32	 **E-1ac**	 **2ac**		-[k]	-[k]
33	 **E-1ad**	 **2ad**		-[k]	-[k]
34	 **E-1ae**	 **2ae**			-[k]

[a] Isolated yields unless otherwise noted. Reaction conditions: Conditions A: 0.27 mmol **1**, mol. 1 mol-% $[Pd(Phen)_2][BF_4]_2$, 1 mol-% $Ru_3(CO)_{12}$, 20 mol-% Phen; mol. 40 µL (0.29 mmol) Et_3N; in butyl formate (10 mL), at 180 °C for 10h. Conditions B: 0.54 mmol **1**, 1 mol-% $Pd(CH_3CN)_2Cl_2$, 2.5 mol-% Phen, 240 µL (2.2 mmol) HCOOPh, 40 µL (0.29 mmol) Et_3N, in CH_3CN (10 mL), 140 °C for 3 h (unless otherwise noted). Conditions C: 0.54 mmol **1**, 1 mol% $Pd(CH_3CN)_2Cl_2$, 5 mol% Phen, 260 µL (2.38 mmol) HCOOPh, 100 µL (0.72 mmol) Et_3N, in CH_3CN + DMF (9+1 mL), at 100 °C for 6 h. Reactions were performed into heavy-wall glass tubes. [b] Determined by GC analysis using biphenyl as the internal standard. [c] **3a**, 20 % yield, was also obtained. [d] Reaction time 4h. [e] Reaction time 8h. [f] Reaction time 12h. [g] Reaction time 5h. [h] Reaction time 6h. [j] Yield measured by ^1H NMR with 2,4-dinitrotoluene as an internal standard. [k] Complex mixture of products. [l] 0.27 mmol of **1y** or **1z** was employed as substrate.

mentioned, Conditions B gave excellent results in many cases, but results are not fully satisfactory for some substrates and in a few cases the reaction yielded mixtures of products in which the target indole was only a minor component. Conditions C finally constitute a marked improvement and allowed to get higher yields of the products in all cases in which a comparison with Conditions B was made.

Coming to the specific functional groups present on the reagent, esters (**1a,c-f**) derived from 2-nitrocinnamic acid were successfully cyclized providing the corresponding indoles in good to excellent yields. Remarkably, a bromine substituent on the aryl ring (**1f**) was well tolerated despite the fact that the presence of the nitro group on the same aryl ring should activate it towards oxidative addition to a low-valent palladium complex. Very likely, the presence of CO inhibits the C-Br oxidative addition.

Amide **1i** afforded somewhat lower yields under Conditions B, but a > 90% yield could be reached under Conditions C. Moving the ester group to the *alpha* position of the starting nitrostyrene (**1j**) lead to a less satisfactory yield. This is the only substrate among those tested for which markedly better results have been previously obtained by using gaseous CO, albeit with much higher catalyst loadings (10-12 mol-%).[3f, 29] Prolonging the reaction time did not improve the yield, indicating that the catalyst deactivates before the end of the reaction. On the other hand, a keto group (**1g**), and even a free aldehydic group (**1h**) were tolerated. Cyclization of **1h** to **2h** by any means has been previously reported only once, using gaseous CO as reductant, using 10 mol-% of a rhodium complex as catalyst and affording a lower (52%) yield with respect to that achieved by us under Conditions C.[3f] Worthy of note, the synthesis of **2h** would not be possible by any alternative reaction employing an arylamine as starting material or in which the arylamine is formed as an intermediate.

Indoles having a cyano group in the position 3 and an aryl group in the position 2 (**2k**-**2m**) were obtained in excellent yield independent of the presence of electronwithdrawing or donating groups on the aryl ring. When a sensitive pyrrole ring was present in the place of the aryl ring (**2n**), the yield was quite lower under Conditions B. However, moving to Conditions C markedly improved the results.

The Z/E nitrostilbene (**Z/E-1b**) mixture gave much better yields under Conditions B than under Conditions A and even better results could be obtained under Conditions C employing the separate isomers. Under these conditions, a complete

conversion was observed for both isomers. However, if the reactions in entries 16 and 17 were run for just 3 h instead of 6, a 64 % conversion of ***E*-1b** was observed, but the conversion of ***Z*-1b** was just 29%. This parallels the lower reactivity of *Z* isomer with respect to the *E* one already observed and discussed above for the $[Pd(Phen)_2][BF_4]_2$:$Ru_3(CO)_{12}$:Phen catalytic system with *n*-butyl formate. However, at variance with the results obtained at 180 °C, no isomerized nitrostilbene was detected in the unreacted substrate, confirming that the previously observed nitrostilbene isomerization was due to the high temperature only. This observation has also a mechanistic implication. If any isomerization of nitrostilbene had been observed even at a temperature low enough that a thermal process can be excluded, this would have implied that the initial nitroarene activation were reversible. That no isomerization of the starting material is observed whereas isomerization clearly occurs during the cyclization is a clear proof that the initial substrate activation by the catalyst is irreversible. This fact may not be surprising, but, to the best of our knowledge, has never been stated before.

Nitrostilbenes substituted with electronwithdrawing groups on either or both aryl rings (**1p**, **1q**, **1s**, **1t**) gave excellent results and the same apply to the 2-pyridyl substituted compound **1x**. The case of **1q** is especially interesting. Two nitro groups are present on the substrate and the one in the *para* position with respect to the vinyl substituent should be the most reactive for steric reasons. Indeed, when 2,4-dinitrotoluene is carbonylated to the corresponding methyl dicarbamate by Pd/Phen catalysts and the reaction is stopped before completion, the nitro group in the position 4 is carbonylated to a quite larger extent than that in the position 2 over a range of experimental conditions.[12c] The fact that in the present case the reactions proceeds selectively on the *ortho* nitro group supports the previous proposal that the olefin groups may coordinate to palladium before the reduction occurs, facilitating and addressing the reaction.[2d, 19]

Electrondonating groups on the aryl ring are known to deactivate the nitro group in these reactions (*vide supra*). Yet, good to excellent results could be obtained not only in the presence of the mildly electrondonating methyl group (**1o**), but even in the presence of dimethylamino (**1r**) or two alkoxy (**1u, 1v**) groups. In this case, use of Conditions C is required or anyway highly preferable.

Noteworthy, 2-phenyl-6-azaindole **2w** was synthetized in very high yield. Azaindoles are a class of nitrogen rich molecules that found broad applications in many fields such as pharmaceuticals and agrochemicals and also exhibits peculiar photophysical properties.[30]

Furthermore, double cyclization of 2,6-*bis*((*E*)-2-nitrostyryl)pyridine (**1y**) led to the formation of 2,6-*bis*(2'-indoyl)pyridine in good yields (**2y**). Compounds of this type have been successfully used as ligands in metal-based phosphorescent and electroluminescent compounds.[31]

When the double cyclization of a non-symmetrically substituted conjugated diene was attempted under Conditions C (0.27 mmol of substrate were used instead of 0.54 to keep the same number of nitro groups as for the other reactions), after the standard 6 h reaction time the main product, isolated in a 61 % yield was that in which cyclization had only occurred on the cyano-substituted side (**2z'**). The recovered unreacted diene accounted for the rest of the mass balance. The doubly-cyclized bis-indole (**2z"**) could be obtained in high yield by increasing the reaction time to 16 h. Interestingly, the product was isolated by simple precipitation from the reaction mixture. A few double cyclizations of non-symmetrically substituted *bis*-(2-nitrophenyl)dienes to give 2-2' indoles have been reported in the literature,[3h] but the reactions were always run to complete conversion of the starting dinitro compound. That the reaction is faster on the side of the cyano-substituted olefin is not surprising, given what discussed earlier in this paper, but the observation that the reactivity difference is large enough to allow for a selective monocyclization is, to the best of our knowledge, an unprecedented observation. This possibility paves the way to following reactions in which the unreacted nitro group is converted into different functionalities, such as an amino or imino group.

The only substrates for which our reaction failed to give clean isolable products under all conditions are those containing a free amino (**1aa**) or phenolic (**1ab**) groups and those in which the double bond is part of an allylic acetate (**1ac**) or allylic alcohol (**1ad**) moiety. The reason for the formation of a mixture of compounds in the first case may be due to the easy reaction of anilines with nitroarenes in the presence of Pd/Phen catalysts and CO to give diarylureas.[26] Indole **2aa** may however be easily obtained by reduction of **2q**[32] and this indirect route is preferable in any case. Indeed, preparation of the starting **1aa** following the only published procedure[33] proceeded in our hands in poor yields, whereas synthesis of **1q** can be easily performed by reacting dinitrotoluene with benzaldehyde in the presence of a base and the reagents are very cheap and available on a multi-ton scale if desired. Allylic acetates are typical substrates for the generation of π-allyl complexes and this is the probable entry to different reactions for **1ac**. Activation of allylic alcohols is usually more difficult, but, on the other hand, alcohols can enter a carbonylation reaction of nitroarene to give carbamates, a reaction that is again very efficiently catalyzed by Pd/Phen complexes.[12a, 34] Note anyway that these compounds are very difficult substrates for this kind of reaction. To the best of our knowledge, cyclization of **1aa** to **2aa** or **1ab** to **2ab** has never been reported by any means, whereas that of **1ab** to **2ab** and **1ac** to **2ac** has been reported in just one case to occur with CO and a rhodium catalyst in low yields (11 and 26% respectively) despite the use of a high rhodium loading (10 mol-%).[3f]

Additionally, the presence of a substituent in the second position *ortho* to the nitro group also blocked the reaction. The sensitivity of this kind of cyclization to steric hindrance in this position is a known problem[3f] and our protocol did not solve it.

It worth noting that in several cases the achieved yields are higher than those previously reported in the literature working under CO pressure in an autoclave. For example, the best yields obtained in the case of compounds **2a**,[3f] **2h,**[3f] **2x**, [9b] **2w**[35] and **2p**[5b] were 83 %, 52 %, 63 %, 87 % and 55 %, respectively. This fact clearly demonstrates that our protocol is an effective alternative to those based on the use of pressurized CO and not simply a second-choice strategy when use of the latter is not possible.

To further assess the synthetic value of our protocols, the scalability of our reaction under both Conditions B and Conditions C was investigated.

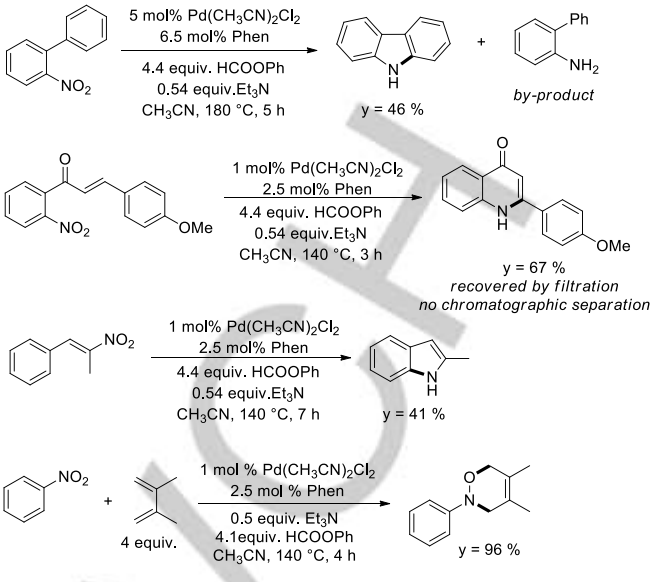
A 14-fold scaled-up reaction (7.5 mmol of the starting material) of **1a** was performed under Conditions B to give **2a** in 84 % isolated yield.

More interestingly, an even larger scale cyclization of **1b** (2.0 g, .8.9 mmol, 16.5-fold scale-up) was performed under

conditions similar to Conditions C, but with half the amount of catalyst (0.5 mol-%) and less solvent (45+5 mL CH_3CN/DMF, 5-fold increase). At the end of the reaction, metallic palladium had been precipitated and the product could be isolated as an analytically and spectroscopically pure compound (1.63 g, 96 % yield) by a simple precipitation and extraction procedure, without the need for any chromatographic purification.

Application to other reductive cyclization reactions of nitro compounds

In order to test the general applicability of our protocol, it was applied to other related reactions. Four reactions were chosen, featuring respectively the functionalization of an aromatic C-H bond,[3r] the formation of a six-membered ring,[3s] the cyclization of a β-nitrostyrene,[3q] and an *inter*-molecular cyclization reaction[3m, 3t] (Scheme 1, paths **f**, **b**, **h**, and **k** respectively and Scheme 4). The protocol worked in all cases even if experimental conditions were not optimized for these specific reactions. Since publication of our preliminary communication on this topic, the synthesis of oxazines has already been the object of a specific study and > 90% yields could be obtained in many cases.[36] Moreover, work is in progress on the synthesis of carbazoles and conditions that allow obtaining these products in excellent yields have been identified.[37] Thus, the use of phenyl formate is not limited to the synthesis of indoles.



Scheme 4. Synthesis of other N-heterocycles (isolated yields are reported).

Kinetic study of phenyl formate decarbonylation and reaction mechanism proposal

In the aim of gaining insight into the reaction mechanism, the decarbonylation step was separately studied. In the previous literature, several papers claim that phenyl formate can be decarbonylated by bases,[25a, 25f, 38] However, one work reported that $Pd(OAc)_2$ in combination with P-based ligands is also able to perform this transformation.[25e]

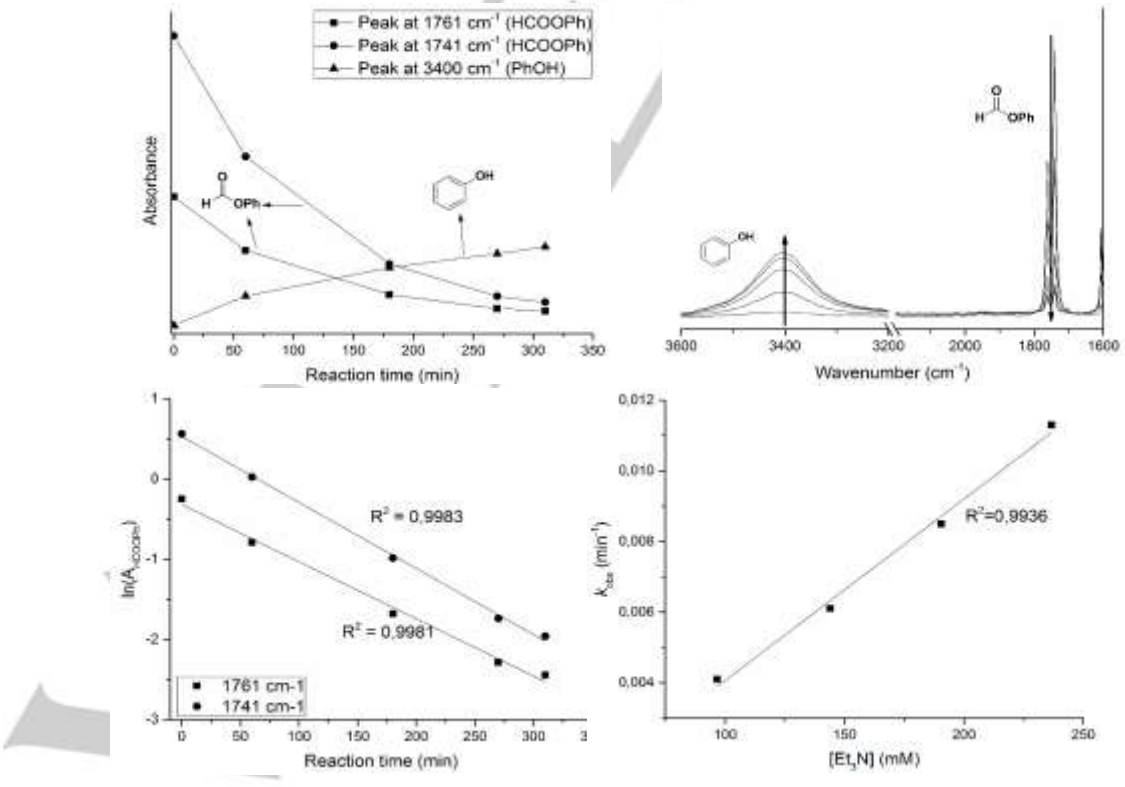


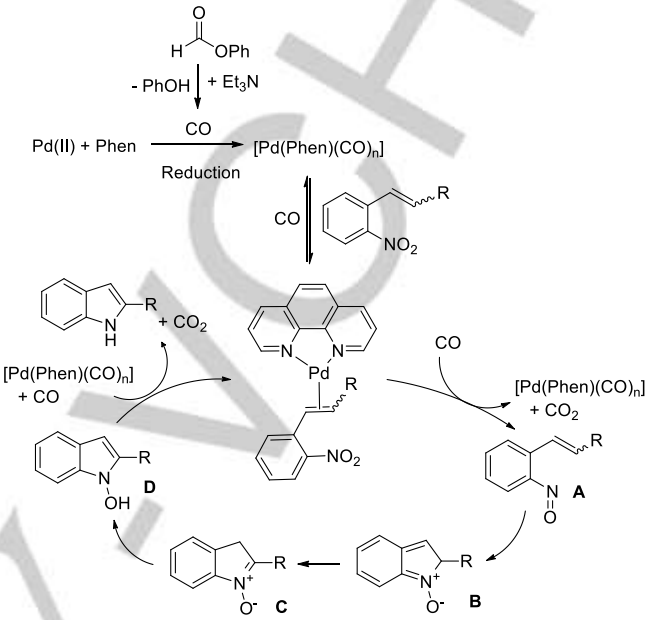
Figure 3. Kinetic analysis of the Et_3N-mediated decarbonylation of phenyl formate in refluxing CH_3CN (for the experimental procedure see Supporting Information).

In order to discriminate between this two kind of activations, HCOOPh was reacted with either 1 equiv. of Et_3N or a catalytic amount of $Pd(CH_3CN)_2Cl_2$ at 140 °C in a pressure tube (Figures S5 and S6). In the first case, a complete conversion to CO and phenol was achieved in 3 h, but no reaction occurred in the presence of $Pd(CH_3CN)_2Cl_2$. A control experiment carried with HCOOPh alone in CH_3CN, ruled out thermal decarbonylation. In addition, phenanthroline, which may also act as a weak base was found to be inactive in the same transformation. All these tests are in accord with the control experiments previously mentioned (Table S3). To track the course of the transformation over time, the reaction of HCOOPh with Et_3N was performed in refluxing CH_3CN and monitored by FT-IR spectroscopy. A decreasing of the two peaks corresponding to the C=O bond was observed over time, accompanied by a parallel increasing of the absorption at 3400 cm^{-1} due to OH stretching in phenol. Noteworthy, no other C=O stretching bands were detected at all stages of the reactions, ruling out the formation of stable intermediates in the reaction, which may affect the kinetic measurement. The reaction rate was found to be first order in both HCOOPh and Et_3N (Figure 3), with a second order constant $k = 5.14\times10^{-2}$ $M^{-1}min^{-1}$ (in CH_3CN at 82 °C). Under the same reaction conditions, *n*-butyl formate was unreactive, indicating a different activation mode.[39]

Finally, the mechanism of the reductive cyclization was considered. Nitrosoarenes are generally considered active intermediates in the reduction of nitro compounds by CO. The intermediate formation of nitrosoarenes in the synthesis of indoles is strongly supported by the very efficient synthesis of oxazines under the same experimental conditions (Scheme 4). We were not able to intercept the nitrosoarene derived from **1a** by addition of a conjugated diene to the reaction mixture. However, this is not surprising because of the high reactivity of nitrosoarenes with olefins[40] and the higher rate of *intra*-molecular reactions with respect to *inter*-molecular ones. As a matter of fact, all previous attempt to obtain *o*-nitrosostyrenes met with failure.[3d, 41]

In the light of the previous experiments and of the results here reported, the following mechanism can be proposed for the present process (Scheme 5). Two independent reactions occur: the phenyl formate decarbonylation and the reductive cyclization. After CO is formed by the Et_3N-mediated decarbonylation reaction, it reduces the starting Pd(II) complex to give a Pd(0) phenanthroline complex, likely coordinated to one or two CO molecules. As discussed above, the starting nitrostyrene appears to coordinate to the zerovalent palladium complex and stabilize it before a reaction with CO results in the formation of *o*-nitrosostyrene **A**. The latter undergoes an *intra*-molecular cyclization affording nitronate **B**, which is converted by a 1,5-H-shift to nitronate **C**. The latter isomerizes to the *N*-hydroxyindole **D** that is finally deoxygenated by a second CO molecule leading to the formation of the indole and the regeneration of the palladium active species. This proposal is supported by experimental[3e] and theoretical evidence.[42]

Note that during the reaction the oxidation state of palladium shuttles between 0 and II. Pd(0) complexes with nitrogen ligands are not stable in the presence of CO, but until the substrate is present, coordination of the double bond and prompt oxidation to Pd(II) prevent the decomposition of the catalyst. Excess phenanthroline also plays an important role in this respect. When the reaction is complete, no oxidant is any longer present and palladium is reduced to palladium black. The appearance of a black ring on the glass tube is a typical indication that the reaction is complete or close to completion.



Scheme 5. Proposed reaction mechanism**.**

Conclusion

In conclusion, we have presented here an efficient, convenient, and general synthetic procedure for the synthesis of nitrogen heterocycles from nitro compounds, based on the use of CO surrogates. The protocol affords the desired products with selectivities and yields that are most often higher than those previously reported using pressurized CO. Additionally, the catalyst (just 1 mol-% or even lesser), the ligand and the CO surrogate are commercially available., thus increasing the user friendliness and the economics of this protocol both on a laboratory and on a larger scale. Worth of note, in at least one case, the indole could be isolated in a pure form and with minimal losses by a simple precipitation/extraction procedure, avoiding the need for a chromatographic purification that would limit the scale on which the reaction can be performed and significantly increase the overall cost of the process.

The decomposition of formates has been investigated. Whereas the presence of a ruthenium catalyst is required to decompose alkyl formates, at least in the absence of very strong bases, organic bases of medium strength are sufficient to catalyze the decomposition of phenyl formate. The kinetics of the reaction was investigated and a first order dependence of the decomposition rate on the base concentration was observed, stressing the need for its presence.[43] [5c, 44]

The apparatus employed and tricks to avoid problems with the O-rings are carefully described in the Experimental Section. This should render it easier to other groups to reproduce our protocol or to extend it to other reactions.

Experimental Section

Apparatus:

In our early experiments, we employed a 18 mL ACE Pressure tube with "front" (inner) seal bushing. This tube has a female-threatened glass end onto which a male-threatened PTFE stopper with a rubber O-ring is placed (Figure S1 left). A weak point of this setting is the rubber O-ring. Those enclosed with the tube or others made of Viton rapidly degraded even during a single run at the temperatures and with the solvents employed in this work, resulting in a pressure drop and possible contamination of the solution by rubber oligomers. Moving to very expensive Karlez O-rings did not solve the problem, neither did employing the tube type with "back" (outer) seal. However, it turned out that the O-ring is not required and simply removing it and hand tightening the stopper provides a good seal. By doing this, the tube can be employed many times. However, upon prolonged (> 50 reactions) use, the PTFE stopper slowly deformed and the tube started to leak. Since the stoppers are not sold separately from the tubes, in the second part of this work we moved to Fisher Scientific heavy walls (2.5 mm) borosilicate glass tubes with Duran PTB screw caps completed with PTFE protected seals (Figure S1 left, Supporting Information). In this case, the seals can be changed independently from the rest of the apparatus. The disadvantage of this apparatus for the occasional user is that the tubes are sold with an open bottom and need to be sealed at the desired length by an experienced glass blower not to compromise the glass strength (the volume of our tubes is 23 mL). Both setups worked well and the choice of which to employ should be based on the type of use foreseen. However, it is important to stress that normal glass should not be employed for these reactions and that care should always be taken in opening the (cold) tubes because residual carbon monoxide pressure is usually present in the tube at the end of the reaction. Heating was performed either by means of an oil bath or by inserting the tubes in a preheated aluminum block in which eight 22.5 mm wide holes had been made to fit the pressure tubes (Figure S1 right). All reactions must be conducted in a well-ventilated hood and a safety screen or other protecting shield should be present during the reaction. We never had problems while performing our reactions, but care must be taken that scratches are not formed on the glass surface that may compromise its resistance. NOTE: ACE 18 mL pressure tube were employed for all reactions involving the use of alkyl formates and for reactions run under Conditions B or during the optimization performed to identify them (results reported in Tables 1, 2, 4, S1, Figures S2-S4, and results for Conditions A and B in Table 9). The following optimization (results in Tables 5-8, S2-S8, and results for Conditions C in Table 9) were performed in Fisher Scientific heavy walls borosilicate 23 mL glass tubes.

General procedure:

Unless otherwise stated, all reactions and manipulations were performed under a dinitrogen atmosphere using standard Schlenk apparatus. All glassware and magnetic stirring bars were kept in an oven at 120 °C for at least two hours and let to cool under vacuum before use. CH_3CN was dried by distillation from CaH_2. DMF was dried by distillation over CaH_2, under reduced pressure at 60 °C. Dried solvents were stored under a dinitrogen atmosphere. Butyl and methyl formate were dried over $MgSO_4$, filtered by cannula techniques and then distilled under a dinitrogen atmosphere. Benzyl formate was degassed by three freeze-pump-thaw cycles but not distilled. Et_3N, DIPEA (*N,N*-diisopropylethylamine), and DBU (1.8-diazabicyclo[5.4.0]undecen-5-ene) were distilled from CaH_2 under reduced pressure. Phenyl formate was purchased form Sigma Aldrich or prepared following a procedure reported in the literature (see Supporting Information). Deuterated solvents were purchased from Sigma-Aldrich: DMSO-d_6 (commercially available in 0.75 mL vials under dinitrogen atmosphere) was used as purchased while $CDCl_3$ was filtered on basic alumina and stored under dinitrogen over 4 Å molecular sieves. 1,10-Phenanthroline (Phen) was purchased as hydrate (Sigma-Aldrich). Before use, it was dissolved in CH_2Cl_2, dried over Na_2SO_4 followed by filtration under a dinitrogen atmosphere and evaporation of the solvent in vacuo. Phen was weighed in the air but stored under dinitrogen to avoid water uptake. All the Pd precursors employed in this work were prepared starting from commercially available $PdCl_2$ following procedures reported in the literature (see Supporting Information). $Ru_3(CO)_{12}$ and the starting nitrostyrenes were synthesized as described in the Supporting Information. All other reagents were purchased from Sigma-Aldrich or Alfa-Aesar and used without further purifications. ^{1}H-NMR and ^{13}C-NMR spectra were recorded at room temperature on a *Bruker Avance DRX 300, Bruker Avance DRX 400 or Bruker Avance 600*. Chemical shifts are reported in ppm relative to TMS. Gas-chromatographic analyses were performed using a *Shimadzu* 2010 gas chromatograph equipped with a Supelco SLB™-5ms capillary column. A standard analysis involves the preparation of a sample solution in CH_2Cl_2 (conc. 0.1 mg/mL^{-1} calculated with respect to biphenyl used as the internal standard). GC-MS analyses were recorded using a *Thermo Fisher ISQ™QD* Single Quadrupole GC-MS equipped with a ZB-1MS 60m column. Elemental analyses were performed on a *Perkin Elmer 2400 CHN* elemental analyzer. IR spectra were registered on a *Varian Scimitar FTS-1000*.

General methods for catalytic reactions

In order to avoid weighing very small amounts of the catalysts, stock solutions (under dinitrogen) of all ruthenium and palladium catalysts were prepared in the appropriate alkyl formate or CH_3CN (in the case of phenyl formate). For catalytic runs that required an amount of Phen less than 10 mg, a stock solution was prepared. For a typical reaction, the pressure tube (see Note in the apparatus section) containing a magnetic stirring bar was charged with the substrate and Phen (when the amount of the latter is larger than 10 mg) and the tube was then immediately placed in a Schlenk tube with a wide mouth. The tube was evacuated and filled with dinitrogen three times to remove any air. The appropriate volume of stock solutions of the catalysts, Phen (if not added as a solid), HCOOPh (if required), the solvent (total solvent amount was 10 mL) and the base were added in this order. It is important that the base is added at the end because in some cases CO evolution may start immediately after its addition even at RT. Then, the reaction vessel was immediately plugged with a PTFE or PTFE-lined screwed-cap and the mixture let to stir for 10 min. This time is required to allow for the coordination of Phen to palladium. Formation of a precipitate of $Pd(Phen)Cl_2$ may be observed depending on the catalyst identity and concentration. This complex is little soluble at RT, but dissolves at higher temperatures and when it reacts to give the catalytically active species. Heating the mixture without waiting for this time results in a lower activity apparently because reduction of uncoordinated palladium by liberated CO causes the formation of inactive aggregates. The tube was then either immersed in a pre-heated oil bath or placed in a preheated custom-made aluminum block with holes fitting the tube width (Figure S1). Reagents amounts and other experimental conditions are reported in the captions to the tables. At the end of the reaction, the pressure tube was lifted and let to cool to room temperature. Then, the screw cap was carefully removed, the excess of CO was vented and the content analyzed by GC (biphenyl as an internal standard), GC-MS or the solvent and excess formate were evaporated and the residue subjected to column chromatography (silica gel) using hexane/CH_2Cl_2 or hexane/AcOEt as the eluent (in both cases, from 1 to 2 % of Et_3N was added to the eluent to partially deactivate acidic sites of silica gel. Failure to do this causes extensive decomposition of most indoles).

The same reaction protocol was employed for running the catalytic test in standard Schlenk glassware.

The large-scale reactions were performed in a 250 mL Fisher-Porter pressure bottle. The reaction for the synthesis of **2a** under conditions B was scaled up by a factor of 14. All the components of the reaction were scaled-up and the product was purified by column chromatography as

described above. The reaction for the synthesis of **2b** under Conditions C was scaled-up 16.5-fold with respect to the substrate (2.0 g, 8.9 mmol) and Et_3N (1.17 g, 1.6 mL, 11.5 mmol), but half the amount of catalyst (0.5 mol-%) and less phenyl formate (3.7 g, 3.3 mL, 30.3 mmol, 3.4 eq instead of 4.4) and solvent (45+5 mL CH_3CN/DMF, 5-fold increase) were employed. To ensure completion of the reaction, the reaction time was increased from 6 to 8 h, although the reaction may had reached completion before. At the end of the reaction, metallic palladium had precipitated on the walls of the bottle. The solution was then filtered through a pad of Celite in a Pasteur pipette by cannula technique to remove even colloidal palladium particles possibly present. The product was then precipitated with water, dissolved in CH_2Cl_2 (50 mL) and washed with a saturated $NaHCO_3$ aqueous solution (3 × 30 mL), brine (1 × 50 mL) and water (1 × 50 mL). The organic phase was then dried over Na_2SO_4, filtered and the solvent was evaporated under vacuum to yield the final product as a white, analytically and spectroscopically pure crystalline solid (1.63 g, 96 % yield), without the need for any chromatographic purification. Phenanthroline and any other by-product present in small amounts remained in solution by this procedure. Elemental analysis calcd for $C_{14}H_{11}N$: C, 87.01; H, 5.74; N, 7.25, found: C, 86.69; H, 5.85; N, 7.44.

Concerning the control reactions conducted in the autoclave using pressurized CO, Phen and the substrate were weighed in the air in a glass liner that was then placed inside a Schlenk tube with a wide mouth under a dinitrogen atmosphere. The tube was evacuated and filled with nitrogen three times to remove any air. The catalyst stock solution ($Pd(CH_3CN)_2Cl_2$ in CH_3CN) and Et_3N were added by volume and the liner was closed with a screw cap having a glass wool-filled open mouth which allows gaseous reagents to exchange. The Schlenk tube was immersed in liquid nitrogen until the solvent froze, evacuated, and filled with dinitrogen three times. The liner was rapidly transferred to a 200 mL stainless steel autoclave equipped with magnetic stirring. The autoclave was then evacuated and filled with dinitrogen three times, charged with CO at RT and subsequently immersed in a pre-heated oil bath. At the end of the reaction, the autoclave was quickly cooled with an ice bath and vented.

Procedure for the FT-IR investigations of the HCOOPh decarbonylation. *Procedure followed under typical catalytic reaction conditions*: HCOOPh (109 µL, 1 mmol) was dissolved in 5 mL of CH_3CN inside a ~ 18 mL ACE pressure tube. Subsequently, the desired reagent (Et_3N or $Pd(CH_3CN)_2Cl_2$) was added. The reaction vessel was plugged with a PTFE screw cap and immersed in a preheated oil bath (140 °C) for 3h. At the end of the reaction, the pressure tube was lifted and let to cool to room temperature. Then, the screw cap was carefully removed and the content analyzed at FT-IR using a 0.1 mm CaF_2 cell for liquid samples.

Procedure followed under refluxing CH_3CN conditions (kinetic analysis): HCOOPh (65.4 µL, 0.6 mmol) was dissolved in CH_3CN (3 mL) inside a Schlenk tube. Subsequently, the desired amount of Et_3N was added. The reaction vessel was immersed into a pre-heated oil bath reaching refluxing conditions. At the desired time, the Schlenk tube was lifted-up and after 5 minutes a very small aliquot was analyzed by FT-IR. The disappearing of HCOOPh was evaluated monitoring the decreasing of the two C=O stretching bands at 1741 cm^{-1} and 1761 cm^{-1}.

Characterization of the products of the catalytic reactions Yields and amounts of the product reported (mg and mmol) refer to the method affording the highest yield (see Table 9 for yields under different experimental conditions).

Methyl 1*H*-indole-2-carboxylate (2a): Obtained as a white solid (90 mg, 0.51 mmol, 95 % yield) after column chromatography (hexane:CH_2Cl_2 = 7:3 + 1 % Et_3N). ^1H NMR (300 MHz, $CDCl_3$) δ 8.98 (br, 1H), 7.70 (d, *J* = 8.1 Hz, 1H), 7.43 (d, *J* = 8.3 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.25 (d, *J* = 8.2 Hz, 1H), 7.16 (t, *J* = 7.5 Hz, 1H), 3.96 ppm (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.85, 137.27, 127.9, 127.5, 125.8, 123.0, 121.2, 112.3, 109.2, 52.4 ppm. Elemental analysis calcd for $C_{10}H_9NO_2$.: C 68.56; H 5.18; N 8.00, found: C 68.50; H 5.23; N 8.01.

2-Phenyl-1*H*-indole (2b): Obtained as a white solid (94 mg, 0.49 mmol, 90 % yield) after column chromatography (hexane:CH_2Cl_2 = 7:3 + 1 % Et_3N). ^1H NMR (300 MHz, $CDCl_3$) δ 8.33 (br, 1H), 7.73 – 7.64 (m, 3H), 7.53 – 7.40 (m, 4H), 7.36 (t, *J* = 7.3 Hz, 1H), 7.25 (dd, *J* = 13.4, 5.3 Hz, 1H), 7.18 (t, *J* = 7.4 Hz, 1H), 6.87 ppm (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.3, 137.3, 132.8, 129.7, 129.4, 128.1, 125.6, 122.8, 121.1, 120.7, 111.3, 100.4 ppm. Elemental analysis calcd for $C_{14}H_{11}N$: C 87.01; H 5.74; N 7.25, found: C 86.85; H 5.80; N 7.30.

Ethyl 1*H*-indole-2-carboxylate (2c): Obtained as a white solid (94 mg, 0.50 mmol, 92 % yield) after column chromatography (hexane:CH_2Cl_2 = 3:7 + 1 % Et_3N). ^1H NMR (400 MHz, $CDCl_3$) δ 8.90 (br, 1H), 7.70 (dd, *J* = 8.1, 0.9 Hz, 1H), 7.43 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.33 (ddd, *J* = 8.3, 7.0, 1.1 Hz, 1H), 7.24 (dd, *J* = 2.1, 1.0 Hz, 1H), 7.16 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 4.42 (q, *J* = 7.1 Hz, 1H), 1.42 ppm (t, *J* = 7.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.0, 136.8, 127.5, 125.3, 122.6, 120.8, 111.8, 108.6, 61.0, 14.4 ppm. Elemental analysis calcd for $C_{11}H_{11}NO_2$: C 69.83; H 5.86; N 7.40, found: C 69.67; H 5.80; N 7.40.

***t*-Butyl-1*H*-indole-2-carboxylate (2d):** Obtained as a white solid (102 mg, 0.46 mmol, 87 % yield) after column chromatography (hexane:AcOEt = 1:1 + 1 % Et_3N). ^1H NMR (300 MHz, $CDCl_3$) δ 8.95 (s, 1H), 7.68 (d, *J* = 8.9 Hz, 1H), 7.42 (d, *J* = 8.3 Hz, 1H), 7.31 (t, *J* = 7.6 Hz, 1H), 7.19 – 7.11 ppm (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.7, 137.0, 129.4, 128.0, 125.4, 122.9, 121.0, 112.2, 108.5, 82.2, 28.7 ppm. Elemental analysis calcd for $C_{13}H_{15}NO_2$: C 71.87; H 6.96; N 6.45, found: C 71.71; H 6.95; N 6.70.

Methyl 6-methyl-1*H*-indole-2-carboxylate (2e): Obtained as a white solid (98 mg, 0.52 mmol, 96 % yield) after column chromatography (hexane:CH_2Cl_2 = 3:7 + 1 % Et_3N). ^1H NMR (600 MHz, $CDCl_3$) δ 8.79 (br, 1H), 7.57 (d, *J* = 8.2 Hz, 1H), 7.19 (d, *J* = 11.6 Hz, 2H), 7.00 (d, *J* = 8.2 Hz, 1H), 3.94 (s, 3H), 2.47 ppm (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.5, 137.4, 135.7, 126.6, 125.4, 123.0, 122.2, 111.5, 108.8, 51.9, 21.9 ppm. Elemental analysis calcd for $C_{11}H_{11}NO_2$: C 69.83; H 5.86; N 7.40, found: C 69.67; H 5.80; N 7.40.

Methyl 6-bromo-1*H*-indole-2-carboxylate (2f): Obtained as a white solid (124 mg, 0.49 mmol, 90 % yield) after column chromatography (hexane:CH_2Cl_2 = 4:6 + 1 % Et_3N). ^1H NMR (600 MHz, $CDCl_3$) δ 8.86 (br s, 1H), 7.59 (s, 1H), 7.55 (d, *J* = 8.6 Hz, 1H), 7.27 (d *J* = 8.6 Hz, 1H), 7.18 (s, 1H), 3.95 ppm (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.0, 137.4, 127.8, 126.3, 124.5, 123.8, 119.2, 114.7, 108.8, 52.1 ppm. Elemental analysis calcd for $C_{10}H_8BrNO$: C 47.27; H 3.17; N 5.51, found: C 47.64; H 3.32; N 5.44.

(1*H*-Indol-2-yl)(phenyl)methanone (2g): Obtained as a white solid (95 mg, 0.43 mmol, 79 % yield) after column chromatography (hexane:AcOEt = 7:3 + 1 % Et_3N). ^1H NMR (300 MHz, $CDCl_3$) δ 9.40 (s, 1H), 8.01 (d, *J* = 7.0 Hz, 2H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.63 (t, *J* = 7.3 Hz, 1H), 7.59 – 7.45 (m, 3H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.22 – 7.13 ppm (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.6, 138.4, 137.9, 134.8, 132.7, 129.6, 128.9, 128.2, 126.9, 123.6, 121.4, 113.1, 112.6 ppm. Elemental analysis calcd for $C_{15}H_{11}NO$: C 81.43; H 5.01; N 6.33, found: C 81.60; H 5.11; N 6.30.

1*H*-Indole-2-carbaldehyde (2h): Obtained as a white solid (51 mg, 0.35 mmol) after column chromatography (hexane:CH_2Cl_2 = 4:6 + 1 % Et_3N). ^1H NMR (400 MHz, $CDCl_3$) δ 9.86 (s, 1H), 9.24 (br, 1H), 7.76 (d, *J* = 8.1 Hz, 1H), 7.47 (d, *J* = 8.3 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.29 (d, 1.8 Hz, 1H), 7.19 ppm (t, *J* = 7.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.0, 138.3, 136.3, 127.7, 127.5, 123.6, 121.5, 114.7, 112.6 ppm. Elemental analysis calcd for C_9H_7NO: C 74.47; H 4.86; N 9.65, found (Conditions B): C 74.30; H 4.55; N 9.60, found (Conditions C): C 74.07; H 4.85; N 9.28.

(1*H*-Indol-2-yl)(piperidin-1-yl)methanone (2i): Obtained as a white solid (112 mg, 0.49 mmol, 91 % yield) after column chromatography (from hexane:CH_2Cl_2 = 1:1 + 1 % Et_3N to hexane:CH_2Cl_2 = 2:8 + 1 % Et_3N). ^1H NMR (400 MHz, $CDCl_3$) δ ^1H NMR (400 MHz, $CDCl_3$) δ 9.22 (br, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.44 (d, *J* = 8.3 Hz, 1H), 7.32 – 7.23 (m, 1H, overlapped with $CDCl_3$), 7.14 (t, *J* = 7.5 Hz, 1H), 6.78 (s, 1H), 3.86 (br, 4H), 1.81 – 1.64 ppm (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 135.7, 129.9, 127.7, 124.3, 121.9, 120.6, 111.8, 104.9, 26.3, 26.2, 24.8 ppm. Elemental analysis calcd for $C_{14}H_{16}N_2O$: C 73.66; H 7.06; N 12.27, found (Conditions B): C 73.76; H 7.20; N 12.01, found (Conditions C): C,73.40; H,7.04; N,11.94.

Methyl 1*H*-indole-3-carboxylate (2j): Obtained as a white solid (62 mg, 0.35 mmol, 64 % yield) after column chromatography (hexane:CH_2Cl_2 =8:2 + 1 % Et_3N). ^1H NMR (400 MHz, $CDCl_3$) δ 8.69 (br, 1H), 8.26 – 8.10 (m, 1H), 7.92 (d, J = 3.0 Hz, 1H), 7.46 – 7.36 (m, 1H), 7.35 – 7.21 (m, 2H), 3.93 ppm (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.6, 136.1, 131.0, 125.8, 123.2, 122.1, 121.5, 111.5, 108.8, 51.1 ppm. Elemental analysis calcd for $C_{21}H_{15}N_3$: C 68.56; H 5.18; N 8.00, found (Conditions B): C 68.75; H 5.03; N 8.24, found (Conditions C):C, 68.48; H, 5.26; N, 7.76.

2-(4-Chlorophenyl)-1*H*-indole-3-carbonitrile (2k): Obtained as a white solid (129 mg, 0.51 mmol, 94 % yield) after column chromatography (hexane:CH_2Cl_2 = 7:3 + 1 % Et_3N). ^1H NMR (600 MHz, DMSO-d_6) δ 12.65 (br, 1H), 8.00 (d, *J* = 8.6 Hz, 2H), 7.72 (d, *J* = 8.6 Hz, 2H), 7.66 (d, *J* = 7.9 Hz, 1H), 7.57 (d, *J* = 8.1 Hz, 1H), 7.34 (t, *J* = 8.1 Hz, 1H), 7.28 ppm (t, *J* = 7.4 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 143.8, 136.1, 135.1, 129.9, 129.2, 128.7, 124.6, 122.6, 118.9, 117.2, 113.2, 82.3 ppm. Elemental analysis calcd for $C_{15}H_9ClN_2$: C 71.29; H 3.59; N 11.09, found: C 71.29; H 3.62; N 10.97.

2-(*p*-Tolyl)-1*H*-indole-3-carbonitrile (2l): Obtained as a white solid (120 mg, 0.52 mmol, 95 % yield) after column chromatography (hexane:CH_2Cl_2 = 7:3 + 1 % Et_3N). ^1H NMR (400 MHz, DMSO-d_6) δ 12.52 (br, 1H), 7.89 (d, *J* = 8.1 Hz, 2H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.44 (d, *J* = 8.0 Hz, 2H), 7.28 (dt, *J* = 22.4, 7.1 Hz, 2H), 2.41 ppm (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 145.4, 140.3, 135.9, 130.3, 128.8, 127.3, 127.0, 124.2, 122.4, 118.7, 117.6, 113.0, 81.4, 21.4 ppm. Elemental analysis calcd for $C_{16}H_{12}N_2$: C 82.73; H 5.21; N 12.06, found: C 82.38; H 5.23; N 11.72.

2-(4-(Diethylamino)phenyl)-1*H*-indole-3-carbonitrile (2m): Obtained as a white solid (149 mg, 0.51 mmol, 95 % yield) after column chromatography (hexane:CH_2Cl_2 = 8:2 + 1 % Et_3N). ^1H NMR (300 MHz, DMSO-d_6) δ 12.19 (br, 1H), 7.84 (d, *J* = 9.0 Hz, 2H), 7. 53 (dd, *J* = 6.6, 1.6 Hz, 1H), 7.47 (dd, *J* = 6.8, 1.6 Hz, 1H), 7.28 – 7.15 (m, 2H), 6.85 (d, *J* = 9.0 Hz, 2H), 3.43 (q, *J* = 7.0 Hz, 4H), 1.14 ppm (t, *J* = 7.0 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 148.9, 146.6, 135.7, 129.12, 128.5, 123.4 122.0, 118.2, 118.1, 115.7, 112.5, 111.8, 78.8, 44.1, 12.9 ppm. Elemental analysis calcd for $C_{19}H_{19}N_3$: C 78.86; H 6.62; N 14.52, found: C 78.87; H 6.60; N 14.50.

2-(1-Methyl-1*H*-pyrrol-2-yl)-1*H*-indole-3-carbonitrile (2n): Obtained as a white solid (92 mg, 0.42 mmol, 77 % yield) after column chromatography (hexane:CH_2Cl_2 = 4:6 + 1 % Et_3N). ^1H NMR (400 MHz, $CDCl_3$) δ 8.59 (br, 1H), 7.75 (m, 1H), 7.44 (m, 1H), 7.36 – 7.26 (m, 2H), 6.89 – 6.82 (m, 1H), 6.58 (dd, *J* = 3.7, 1.7 Hz, 1H), 6.28 (dd, *J* = 3.7, 2.8 Hz, 1H), 3.85 ppm (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2, 134.8, 128.6, 126.8, 124.3, 122.9, 122.5, 119.5, 116.9, 112.7, 111.7, 109.3, 85.3, 35.8 ppm. Elemental analysis calcd for $C_{14}H_{11}N_3$: C, 76.00; H, 5.01; N, 18.99, found (Conditions B): C 76.25; H 5.13; N 18.70, found (Conditions C): C, 76.38; H, 5.24; N, 18.69

6-Methyl-2-phenyl-1*H*-indole (2o): Obtained as a white solid (107 mg, 0.52 mmol, 96 % yield) after column chromatography (hexane:AcOEt = 85:15 + 1 % Et_3N). ^1H NMR (400 MHz, $CDCl_3$) δ 8.19 (br, 1H), 7.65 (d, *J* = 7.7 Hz, 2H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.44 (t, *J* = 7.7Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 1H), 7.19 (s, 1H), 6.97 (d, *J* = 8.0 Hz, 1H), 6.79 (d, 1.0 Hz, 1H), 2.48 ppm (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.7, 137.6, 132.9, 132.7, 129.4, 127.9, 127.5, 125.4, 122.5, 120.7, 111. 3, 100.2, 22.2 ppm. Elemental analysis calcd for $C_{15}H_{13}N$: C 86.92; H 6.32; N 6.76, Found: C 86.85; H 6.40; N 6.51.

2-Phenyl-6-(trifluoromethyl)-1*H*-indole (2p): Obtained as a white solid (139 mg, 0.53 mmol, 98 % yield) after column chromatography (hexane:CH_2Cl_2 =8:2 + 1 % Et_3N). ^1H NMR (600 MHz, $CDCl_3$) δ 8.55 (br, 1H), 7.71-7.68 (m, 4H), 7.48 (t, *J* = 7.7 Hz, 2H), 7.40-7.36 (m, 2H), 6.88 ppm (d, *J* = 1.7 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 140.6, 135.6, 131.60, 131.57 129.2, 128.5, 125.4, 125.2 (q, $^1J_{CF}$ = 271.5 Hz), 124.2 (q, $^2J_{CF}$ = 32.2 Hz), 120.9, 117.02 (q, $^3J_{CF}$ = 3.4 Hz), 108.4 (q, $^3J_{CF}$ = 4.3 Hz), 100.1 ppm. ^{19}F NMR (282 MHz, $CDCl_3$) δ -60.96 ppm (s). Elemental analysis calcd for $C_{15}H_{10}F_3N$: C 68.96; H 3.86; N 5.36, found: C 68.70; H 3.66; N 5.15.

6-Nitro-2-phenyl-1H-indole (2q): Obtained as a white solid (100 mg, 0.42 mmol, 78 % yield) after column chromatography (hexane:AcOEt = 70:30 + 1 % Et_3N). ^1H NMR (400 MHz, DMSO-d_6) δ 12.34 (br, 1H), 8.29 (d, *J* = 1.8 Hz, 1H), 7.94 (d, *J* = 7.4 Hz, 2H), 7.91 (dd, *J* = 8.8, 2.1 Hz, 1H), 7.72 (d, *J* = 8.8 Hz, 1H), 7.54 (t, *J* = 7.7 Hz, 2H), 7.43 (t, *J* = 7.4 Hz, 1H), 7.15 ppm (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 144.0, 141.7, 135.2, 133.5, 130.6, 129.0, 128.8, 125.6, 119.9, 114.6, 107.6, 99.7 ppm. Elemental analysis calcd for $C_{14}H_{10}N_2O_2$: C, 70.58; H, 4.23; N, 11.76, found: C,70.78; H,4.27; N,11.46.

***N*,*N*-Dimethyl-2-phenyl-1*H*-indol-6-amine (2r):** Obtained as a white solid (77 mg, 0.33 mmol, 60 % yield) after column chromatography (hexane:AcOEt = 80:20 + 1 % Et_3N). ^1H NMR (400 MHz, $CDCl_3$) δ 8.15 (br, 1H), 7.61 (d, *J* = 7.9 Hz, 2H), 7.49 (d, *J* = 8.6 Hz, 1H), 7.41 (t, *J* = 7.7 Hz, 2H), 7.27 (t, *J* = 7.3 Hz, 1H, overlapped with $CDCl_3$), 6.82 – 6.70 (m, 3H), 2.98 ppm (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.1, 138.6, 136.0, 132.9, 129.1, 127.0, 124.6, 121.8, 121.1, 110.1, 99.9, 94.9, 42.1 ppm. Elemental analysis calcd for $C_{16}H_{16}N_2$: C, 81.32; H, 6.82; N, 11.85, found: C,81.23; H,7.06; N,11.49.

6-Chloro-2-(4-chlorophenyl)-1*H*-indole (2s): Obtained as a white solid (131 mg, 0.50 mmol, 92 % yield) after column chromatography (hexane:CH_2Cl_2 =7:3 + 1 % Et_3N). ^1H NMR (400 MHz, $CDCl_3$) δ 8.28 (br, 1H), 7.63 – 7.52 (m, 3H), 7.48 – 7.36 (m, 3H), 7.12 (d, *J* = 8.4 Hz, 1H), 6.79 ppm (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.43, 137.19, 133.78, 130.42, 129.31, 128.37, 127.73, 126.31, 121.56, 121.25, 110.88, 100.42 ppm. Elemental analysis calcd for $C_{14}H_9Cl_2N$: C 64.15; H 3.46; N 5.34, found: C 64.50; H 3.66; N 5.15.

2-(2-Chlorophenyl)-1*H*-indole (2t): Obtained as a white solid (116 mg, 0.51 mmol, 64 % yield) after column chromatography (hexane:CH_2Cl_2 =7:3 + 1 % Et_3N); 94 % yield. ^1H NMR (300 MHz, $CDCl_3$) δ 8.78 (br, 1H), 7.78 – 7.66 (m, 1H), 7.56 – 7.51 (m, 1H), 7.46 (d, *J* = 8.1 Hz, 1H), 7.39 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.34 (dd, *J* = 5.3, 1.7 Hz, 1H), 7.32 – 7.27 (m, 1H), 7.24 – 7.15 (m, 1H), 6.92 ppm (d, *J* = 1.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.8, 135.5, 131.8, 131.6, 131.2, 131.1, 129.2, 128.6, 127.7, 123.1, 121.2, 120.6, 111.5, 104.0 ppm. Elemental analysis calcd for $C_{14}H_{10}ClN$: C 73.85; H 4.43; N 6.15, found: C 73.50; H 4.66; N 6.01.

5,6-Dimethoxy-2-phenyl-1*H*-indole (2u): Obtained as a white solid (97 mg, 0.38 mmol, 71 % yield) after column chromatography (hexane:AcOEt = 75:25 + 1 % Et_3N). ^1H NMR (400 MHz, $CDCl_3$) δ 8.21 (br, 1H), 7.64 – 7.58 (m, 2H), 7.44 – 7.38 (m, 2H), 7.29 (m, 1H overlapped with residual solvent signal), 7.08 (s, 1H), 6.91 (s, 1H), 6.73 (dd, *J* = 2.2, 0.8 Hz, 1H), 3.93 ppm (d, *J* = 5.6 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.5, 145.6, 136.7, 132.8, 131.5, 129.1, 127.2, 124.7, 122.3, 102.4, 100.0, 94.6, 56.5, 56.3 ppm. Elemental analysis calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53, found: C, 75.49; H, 6.09; N, 5.19.

6-Phenyl-5*H*-[1,3]dioxolo[4,5-*f*]indole (2v): Obtained as a yellow solid (92 mg, 0.39 mmol, 72 % yield) after column chromatography (hexane:AcOEt = 70:30 + 1 % Et_3N). ^1H NMR (400 MHz, DMSO-d_6) δ

11.37 (s, 1H), 7.75 (d, *J* = 7.4 Hz, 2H), 7.41 (t, *J* = 7.7 Hz, 2H), 7.24 (t, *J* = 7.4 Hz, 1H), 6.99 (s, 1H), 6.90 (s, 1H), 6.75 (d, *J* = 1.8 Hz, 1H), 5.94 ppm (s, 2H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 144.1, 142.2, 136.0, 132.3, 131.9, 128.7, 126.5, 124.1, 122.3, 99.98, 98.95, 98.3, 91.8 ppm. Elemental analysis calcd for $C_{15}H_{11}NO_2$: C, 75.94; H, 4.67; N, 5.90, found: C, 75.69; H, 4.71; N, 5.55.

2-Phenyl-6-azaindole (2w): Obtained as a white solid (95 mg, 0.49 mmol, 91 % yield) after column chromatography (AcOEt + 2 % Et_3N + 1 % MeOH). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.27 (br, 1H), 8.96 (s, 1H), 8.27 (d, *J* = 5.5 Hz, 1H), 7.82 (d, *J* = 7.3 Hz, 2H), 7.63 – 7.36 (m, 4H), 6.85 ppm (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.4, 138.8, 134.3, 134.1, 133.8, 129.2, 128.8, 126.0, 115.1, 98.9 ppm. Elemental analysis calcd for $C_{13}H_{10}N_2$: C 80.39; H 5.19; N 14.42, found: C 80.29; H 4.98; N 14.23.

2-(Pyridin-2-yl)-1*H*-indole (2x): Obtained as a white solid (103 mg, 0.53 mmol, 98 % yield) after column chromatography (hexane:CH_2Cl_2 = 7:3 + 1 % Et_3N). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.75 (br, 1H), 8.58 (d, *J* = 4.6 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.73 (td, *J* = 7.8, 1.7 Hz, 1H), 7.66 (d, *J* = 7.9 Hz, 1H), 7.42 (d, *J* = 8.2 Hz, 1H), 7.26-7.16 (m, 2H, overlapping with $CDCl_3$), 7.12 (t, *J* = 7.5 Hz, 1H), 7.04 ppm (d, *J* = 1.1 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.5, 149.04, 137.4, 137.1, 136.6, 129.4, 123.8, 122.4, 121.3, 120.6, 120.4, 111.9, 101.4 ppm. Elemental analysis calcd for $C_{13}H_{10}N$: C 80.39; H 5.19; N 14.42, found: C 80.19; H 5.23; N 14.35.

2,6-Di(1*H*-indol-2-yl)pyridine (2y): Obtained as a white solid (65 mg, 0.21 mmol, 78 % yield) after column chromatography (hexane:CH_2Cl_2 =7:3 + 1 % Et_3N). ^{1}H NMR (300 MHz, DMSO-*d*$_6$) δ 11.71 (s, 1H), 7.88 (t, 2H), 7.61 (dd, *J* = 17.9, 8.0 Hz, 4H), 7.28 (d, *J* = 1.2 Hz, 2H), 7.25 – 7.18 (m, 2H), 7.07 ppm (t, *J* = 7.1 Hz, 2H). ^{13}C NMR (75 MHz, DMSO-*d*$_6$) δ 150.3, 138.7, 137.9, 137.6, 129.5, 123.6, 121.8, 120.5, 118.7, 112.4, 101.7 ppm. Elemental analysis calcd for $C_{21}H_{15}N_3$: C 81.53; H 4.89; N 13.58, found: C 81.75; H 4.83; N 13.34.

(*E*)-2-(2-Nitrostyryl)-1*H*-indole-3-carbonitrile (2z'): Obtained as a yellow solid (48 mg, 0.17 mmol, 61 % yield) after column chromatography (hexane:CH_2Cl_2 = 40:60 + 1 % Et_3N). The yield reported in table 9 was calculated considering the molecular weight of the hemihydrate molecule. ^{1}H NMR (300 MHz, DMSO-*d*$_6$) δ 12.62 (br, 1H), 8.11 (d, *J* = 7.6 Hz, 1H), 8.05 (dd, *J* = 8.1, 0.9 Hz, 1H), 7.83 (d, *J* = 16.3 Hz, 1H, olefinic CH overlapped with multiplet at 7.84 – 7.76), 7.84 – 7.76 (m, 1H), 7.67 – 7.58 (m, 2H), 7.54 (d, *J* = 8.1 Hz, 1H), 7.320(d, *J* = 16.3 Hz, 1H, olefinic CH overlapped with multiplet at 7.39 – 7.31), 7.39 – 7.31 (m, 1H), 7.28 – 7.21 ppm (m, 1H). ^{13}C NMR (75 MHz, DMSO-*d*$_6$) δ 148.1, 142.4, 136.1, 133.7, 130.2, 129.8, 128.3, 127.4, 127.1, 124.9, 124.6, 122.1, 119.8, 118.6, 115.7, 112.51, 85.25 ppm. MS (ESI+), *m/z* $[M+Na]^+$ calcd for $C_{17}H_{11}N_3NaO_2^+$: 312.07, found 312.32. MS (ESI-), *m/z* $[M-H]^-$ calcd for $C_{17}H_{10}N_3O_2^-$: 289.08, found 288.57. Elemental analysis calcd for $C_{17}H_{11}N_3O_2 \cdot ½\ H_2O$: C, 68.45; H, 4.05; N, 14.09, found: C, 68.58; H, 4.61; N, 14.09.

1*H*,1'*H*-[2,2'-Biindole]-3-carbonitrile (2z''): Obtained as a white solid (62 mg, 0.24 mmol, 90 % yield) and recovered without column chromatography. The product was precipitated from the reaction mixture by addition of water (15 mL), collected by filtration on a Buchner funnel, let to dry on the filter paper and then washed several times with mixture of hexane and CH_2Cl_2 (3:1). ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 12.42 (br, 1H), 11.54 (br, 1H), 7.69 (d, *J* = 7.9 Hz, 1H), 7.65 (d, *J* = 7.7 Hz, 1H), 7.59 (d, *J* = 7.9 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.33 (dd, 7.2, 1.2 Hz, 1H), 7.30 – 7.21 (m, 2H, partially overlapped with singlet at 7.21), 7.21 (s, 1H), 7.11 ppm (t, *J* = 7.9 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ 138.2, 137.1, 135.3, 128.0, 127.9, 127.3, 123.9, 123.3, 122.2, 120. 9, 120.3, 118.2, 116.6, 112.6, 112.0, 103.3, 81.1 ppm. MS (ESI-), *m/z* $[M-H]^-$ calcd for $C_{17}H_{10}N_3^-$: 256.09, found 256.43. Elemental analysis calcd for $C_{17}H_{11}N_3$: C, 79.36; H, 4.31; N, 16.33, found: C, 78.98; H, 4.65; N, 15.97.

2-(4-Methoxyphenyl)quinolin-4(1*H*)-one: After the catalytic reaction, a white solid precipitated from the mixture . It was filtered through Büchner funnel, washed with cold acetonitrile and dried under vacuum (91 mg, 0.36 mmol, 67 % yield). ^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 11.57 (br, 1H), 8.09 (d, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 8.7 Hz, 2H), 7.77 (d, *J* = 8.3 Hz, 1H), 7.66 (t, *J* = 7.3 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.15 (d, *J* = 8.7 Hz, 2H), 6.31 (s, 1H), 3.86 ppm (s, 3H). ^{13}C NMR (151 MHz, DMSO-*d*$_6$) δ 177.3, 161.5, 150.1, 141.0, 132.1, 129.3, 126.7, 125.3, 125.2, 123.5, 119.1, 114.9, 107.0, 55.9 ppm. Elemental analysis calcd for $C_{16}H_{13}NO_2$: C 76.48; H 5.21; N 5.57, found: C 76.28; H 4.96; N 5.51.

Carbazole: Obtained as a white solid (42 mg, 0.25 mmol, 46 % yield) after column chromatography (hexane:AcOEt=8:2 + 1 % Et_3N). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (d, *J* = 7.8 Hz, 1H), 7.99 (br, 1H), 7.48 – 7.40 (m, 2H), 7.32 – 7.17 ppm (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.9, 126.2, 123.7, 120.7, 119.8, 111.0 ppm. Elemental analysis calcd for $C_{12}H_9N$: C 86.20; H 5.43; N 8.38, found: C 86.30; H 5.35; N 8.35.

2-Methylindole: Obtained from β-nitrostyrene (29 mg, 0.22 mmol, 41 % yield) after column chromatography (hexane:CH_2Cl_2=7:3 + 1 % Et_3N). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (br, 1H), 7.54 (d, *J* = 7.5 Hz, 1H), 7.29 (d, *J* = 7.2 Hz, 1H), 7.18 – 7.05 (m, 2H), 6.22 (s, 1H), 2.45 ppm (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.5, 135.5, 129.5, 121.4, 120.1, 110.7, 100.7, 14.1 ppm. Elemental analysis calcd for C_9H_9N: C 82.41; H 6.92; N 10.68, found: C 82.38; H 6.87; N 10.65.

4,5-Dimethyl-2-phenyl-3,6-dihydro-2*H*-1,2-oxazine: Obtained as a white solid (98 mg, 0.52 mmol, 96 % yield) after column chromatography (hexane:CH_2Cl_2 =7:3 + 1 % Et_3N). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (t, *J* = 10.6 Hz, 2H), 7.16 (dd, *J* = 11.4, 1.1 Hz, 2H), 7.02 (t, *J* = 9.7 Hz, 1H), 4.35 (s, 2H), 3.69 (s, 2H), 1.76 (s, 3H), 1.67 ppm (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.8, 129.2, 125.4, 122.8, 122.7, 116.3, 72.4, 56.8, 16.3, 14.06 ppm. Elemental analysis calcd for $C_{12}H_{15}NO$: C 76.16; H 7.99; N 7.40, found: C 76.36; H 8.10; N 7.40.

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[39] Since the submission of our preliminary communication on this topic, Manabe and coworkers have published an in depth study of aryl

formate decomposition by bases.[38] Their results are in full agreement with ours. Moreover, the fact that pyridine was found to be the least effective of all the bases tested supports our result that the small amount of phenanthroline present in our system has no significant role in catalyzing phenyl formate decomposition.

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[43] In at least two cases [5c, 44] since the publishing of our preliminary communication on this topic, the use of phenyl formate was compared with that of $Mo(CO)_6$ in reductive cyclization reactions of nitro compounds and in both cases the latter afforded better results. However, in neither case was a base added to the reaction mixture. In our view, this makes the comparison completely meaningless.

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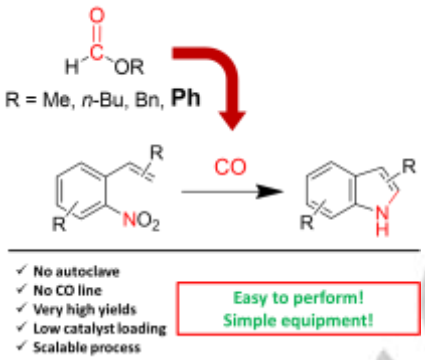

We here describe a very efficient, general and scalable protocol for the preparation of indoles and other *N*-heterocycles from suitably substituted nitroarenes using alkyl and phenyl formates as CO surrogates. Using phenyl formate, the products were isolated in yields often higher than those previously achieved by using gaseous CO. The mechanism of both the decarbonylation reaction of phenyl formate and the cyclization reaction were clarified by kinetic and mechanistic studies.