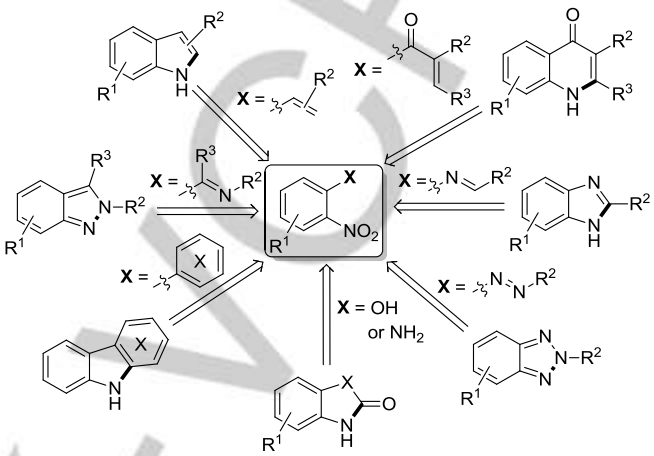
Synthesis of N-Heterocycles by Reductive Cyclization of Nitro Compounds Using Formate Esters as CO Surrogates

Dario Formenti,[a, b] Francesco Ferretti,[a, b] Fabio Ragaini* [a]

Abstract: A series of alkyl and aryl formate esters were evaluated as CO sources in the Pd- and Pd/Ru-catalyzed reductive cyclization of substituted nitro compounds to afford heterocycles, especially indoles. Phenyl formate was found to be the most effective, allowing to obtain the desired products in excellent yields, often higher than those previously reported with pressurized CO. Detailed experiments and kinetic studies discern between a metal-catalyzed and a base-mediated activation of phenyl formate confirming that just the base is effective in catalyzing its decarbonylation.

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. In particular, during the years, a plethora of nitrogen containing heterocycles have been prepared from suitably *ortho*-substituted nitroarenes using CO as a stoichiometric reductant (Scheme 1) and examples of *inter*-molecular reactions and of reactions employing β-nitrostyrenes and related molecules as reagents are also known.[3] Despite the high efficiency of several of these reactions, their use has not spread outside the limited number of groups that reported them. This is likely mostly due to the fact that they generally involve the use of pressurized CO, requiring safety measures that are not available in most synthetic organic laboratories. To overcome this limitation and allow more researchers to use this chemistry, several years ago we started investigating the use of molecules capable of releasing CO *in situ*, thus avoiding the need for high pressure equipment and CO lines. Among several suitable reagents,[4] we chose to employ formate esters because of their commercial availability, low cost and low toxicity and selected the Pd-catalyzed synthesis of indoles from *o*-nitrostyrenes (Scheme 1, upper left) as the first reaction to test. We also chose to operate in a single glass pressure tube because this equipment is cheap and available in different sizes. A steel autoclave can also be used, but without the need for pressurized CO. Some of the aforementioned CO-releasing reagents require the use of two-chamber reactors to separate the CO-releasing reaction from the carbonylation one. When we started this study, no alternative had been reported to the use of gaseous CO in nitroarene cyclization reactions. Very recently, Driver and co-workers reported on the use of $Mo(CO)_6$ to this aim.[5] However, the toxicity of this CO source is remarkable and could create complications if used on a larger scale.

Owing to its very low cost, our initial investigation was devoted to prove if *n*-butyl formate could be a successful CO surrogate in the reductive cyclization of methyl (*E*)-2-nitrocinnamate **1a**.



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

$Ru_3(CO)_{12}$ and $[Pd(Phen)_2][BF_4]_2$ were chosen as catalysts for preliminary studies. Indeed, $Ru_3(CO)_{12}$ was extensively employed in decarbonylation reactions of alkyl formates[6] while $[Pd(Phen)_2][BF_4]_2$ is active in the reductive cyclization of aromatic nitro compounds using gaseous CO as the reductant.[2d, 3m, 3p, 3r] Results are summarized in Table S1. The reaction conducted with palladium only proceeded to a small extent (Table S1, entry 4). In contrast, the use of $Ru_3(CO)_{12}$ alone was found to be effective showing a fair selectivity towards indole but only a moderate conversion of the nitrostyrene (Table S1, entry 5). The combination of the two metals allowed for an increased yield (Table S1, entry 6). Organic bases accelerate the reaction (Table S1, entries 9, 10, 11), but only Et_3N was able to increase the selectivity towards the desired indoles **2a** (Table S1, compare entry 6 with entry 7). However, when Et_3N was used, 2-ethyl-indolecarboxylate, **3a,** was also produced. An elongation of the reaction time allowed for a higher conversion and an increased selectivity in both indole **2a** and **3a**. Under the same reaction conditions, benzyl and methyl formate did not afford better results (Table S1, entries 12 and 13, respectively). In the case of *n*-butyl, methyl and benzyl formate, the main side product was represented by methyl 2-aminocinnamate. Its formation can be explained by a Ru-mediated reduction of nitro group.[7] Surprisingly, when phenyl formate was employed, complete conversion and a moderate selectivity was achieved (Table S1, entry 14). Gratefully, if the reaction temperature was decreased from 180 °C to 140 °C, selectivity increased to 92% (Table S2, entry 2). Spurred by these encouraging results, we focused our efforts to optimize the desired transformation using HCOOPh as the CO source.[8]

Our investigation started with the evaluation of various Pd

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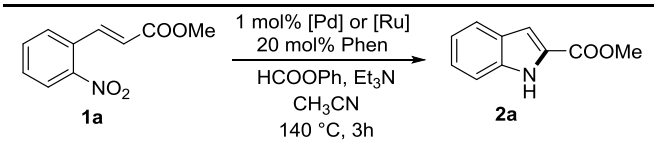
Supporting information for this article is given via a link at the end of the document.

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



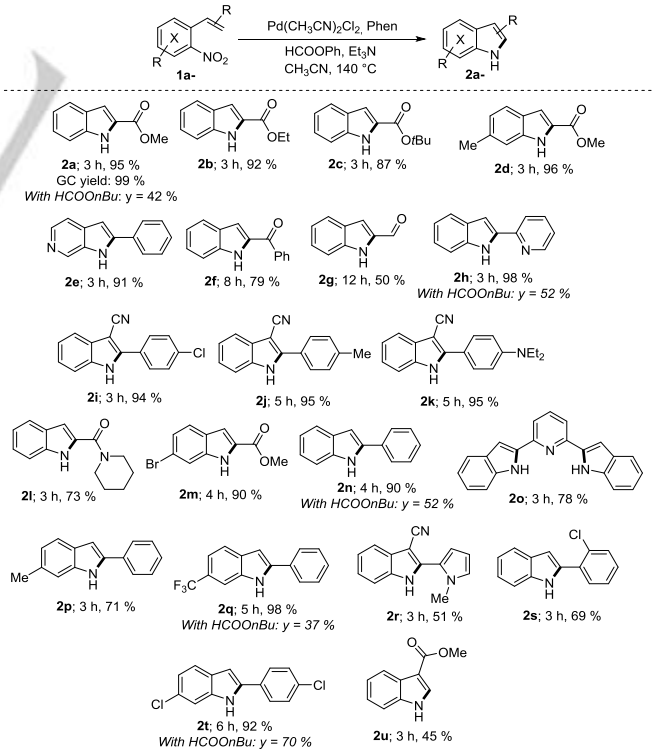
Entry	Catalyst	**1a** Conversion [%][b], [c]	**2a** Selectivity [%][b], [c]
1	$Pd(CH_3CN)_2Cl_2$	>99 (19)	98 (17)
2	$[Pd(Phen)_2][BF_4]_2$	>99 (32)	94 (34)
3	$Pd(OAc)_2$	>99 (4)	92 (traces)
4	$Pd(dba)_2$	86 (4)	93 (traces)
5	$Ru_3(CO)_{12}$	23	79
6[d]	$Pd(CH_3CN)_2Cl_2$	58	95

[a] Reaction conditions: 0.27 mmol **1a**, 1 mol% of Pd catalyst 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), 10 mL of CH_3CN. Reactions were performed into heavy-wall borosilicate glass tubes (ACE Pressure tube) at 140 °C for 3 h. [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 an autoclave under CO, 30 bar pressure. No HCOOPh was added. See caption to Scheme 2 for experimental conditions.

sources (Table 1). In all cases, the employed Pd compounds were very effective in the transformation, leading to complete conversion and nearly complete selectivity towards **2a** in the case of $Pd(CH_3CN)_2Cl_2$.

Notably, if the reactions were conducted in the absence of Phen, conversions and selectivities were poor. In contrast to the *n*-butyl formate based protocol, the addition of $Ru_3(CO)_{12}$ does not lead to any improvement (Table S2). Owing to the relatively higher cost of phenyl formate compared to alkyl formates, its amount was optimized. As shown in Figure S2, the reaction maintains its efficiency down to a formate amount 3.4 fold the stoichiometric amount with respect to the required CO (2 equivalents of CO are needed). Further diminishing of the HCOOPh amount led to a slight decrease of the selectivity and a drop in the conversion. Carrying on the optimization, we found that just 1 equivalent of Et_3N is needed to achieve complete conversion and selectivity (Figure S3). Finally, Phen amount was optimized allowing to lower its amount to 5 mol % (Figure S4). Control experiments revealed that the reaction does not proceed in the absence of any among Pd, Et_3N and the CO source (Table S3). Additional experiments demonstrated that if the reaction was conducted into Schlenk glassware connected to a nitrogen line, a poor conversion was achieved (Figure S1). Indeed, after 9 h conversion was only 8%. However, when further 200 µL of HCOOPh were added, the reaction was speeded-up reaching 19% conversion. As the comparison, performing the reaction into a pressure tube at the same temperature, 65% conversion and 97% selectivity were achieved after 9 h. This experiment proves that the sluggish reactivity in an open vessel system cannot be imputed to a deactivation of the Pd catalysts but to a very low CO concentration in the liquid phase. As a matter of fact, pressure tubes are crucial to maximize the amount of CO in solution. In the aim of handling suitable amounts of both starting materials and reaction products the reaction was scaled-up by a factor of two. In order not to shift the coordination equilibria in the system: a) the catalyst and nitroarene amounts were doubled; b) the Phen, Et_3N and CH_3CN amounts were left unvaried; c) the amount of HCOOPh was varied in such a way that its excess with respect to the stoichiometrically required amount remained unchanged. Under these conditions, complete conversion of **1a** and complete selectivity (GC analysis) in **2a** were achieved.

With the best conditions in our hands, the reaction scope was explored (Scheme 2). Esters (**1a**-**c**) and amides (**1l**) derived from 2-nitrocinnamic acid were successfully cyclized providing the corresponding indoles in good to excellent yields. Indoles substituted in 2 and 3 positions with aryl (**2n**), 2-pyridyl (**2h**) and cyano groups (**2i-k**) were also successfully obtained in excellent yields. Labile bromo (**2m**), chloro (**2s**, **2t**, **2i**) and aldehydic (**1g**) groups were well-tolerated. Noteworthy, 2-phenyl-6-azaindole **2e** 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.[9] Furthermore, double cyclization of 2,6-*bis*((*E*)-2-nitrostyryl)pyridine (**1o**) led to the formation of 2,6- bis(2'-indoyl)pyridine in good yields (**2o**).

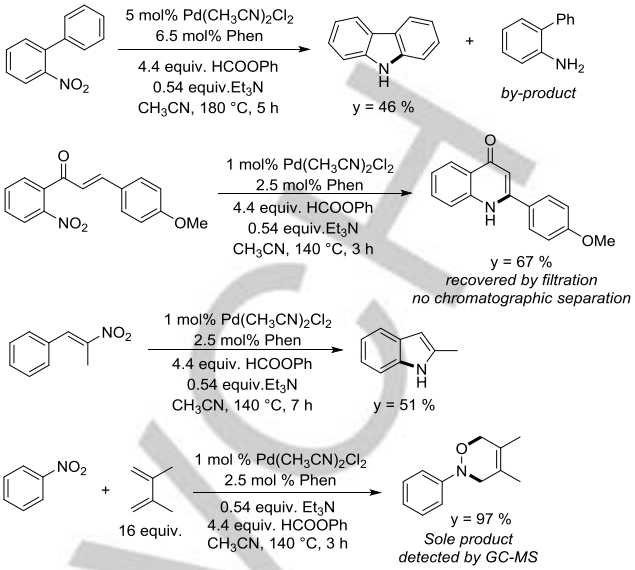


Scheme 2. Substrate scope. Reaction conditions: 0.54 mmol nitroarene, 1 mol % $Pd(CH_3CN)_2Cl_2$, 2.5 mol % Phen, 2.2 mmol HCOOPh, 0.27 mmol Et_3N, 140 °C. Reactions were performed in an ACE Pressure Tube. Yields refer to isolated products.

Compounds of this type have been successfully used as ligands in metal-based phosphorescent and electroluminescent compounds.[10] Lastly, also trifluoromethyl groups were excellently tolerated giving rise to the corresponding indoles in almost quantitative yield. As a comparison, if the previously investigated protocol based on *n*-butyl formate was applied, lower yields were achieved (see compounds **2a**, **2h**, **2n**, **2q** and **2t**) thus confirming the effectiveness of phenyl formate as CO source.[11] Worth of mention, in several cases the achieved yields are higher than those previously reported in the literature using pressurized CO. For example, the best yields obtained in the case of compounds **2a**,[3f] **2h**, [12] **2e**[13] and **2q**[5b] were 83 %, 63 %, 87 % and 55 %, respectively. This fact clearly demonstrates that our protocol is a virtuous alternative to those based on the use of pressurized CO. Indeed, if the model reaction was conducted under CO pressure using optimized conditions (see caption to Scheme 2), but omitting the phenyl formate, a decreased activity was registered and the desired product was obtained in a very high selectivity, but with only a moderate conversion of the starting nitro compound (entry 6 in Table 1).

In addition, we also investigated the scalability of our reaction. A 14-fold scaled-up reaction (7.5 mmol of the starting material) of **1a** was performed to give to give **2a** in 84 % isolated yield.

The developed protocol was applied to other related reactions, to test its general applicability. Four reactions were chosen, featuring respectively the functionalization of an aromatic C-H bond,[3s] the formation of a six-membered ring,[3t] the cyclization of a β-nitrostyrene,[3r] and an *inter*-molecular cyclization reaction[3m, 3u] (Scheme 3). The protocol worked in all cases despite the fact that experimental conditions were not optimized for these specific reactions. Wide margins for improvement clearly exist, but the oxazine yield is already higher than that previously obtained using pressurized CO.



Scheme 3. Synthesis of other N-heterocycles (isolated yields are reported).

In order to gain insight into the reaction mechanism, the decarbonylation step was independently studied. Various previous works in the literature claimed that phenyl formate can be decarbonylated by bases.[8a, 8f] However, one work reported that $Pd(OAc)_2$ in combination with P-based ligands is also able to perform this transformation.[8e]

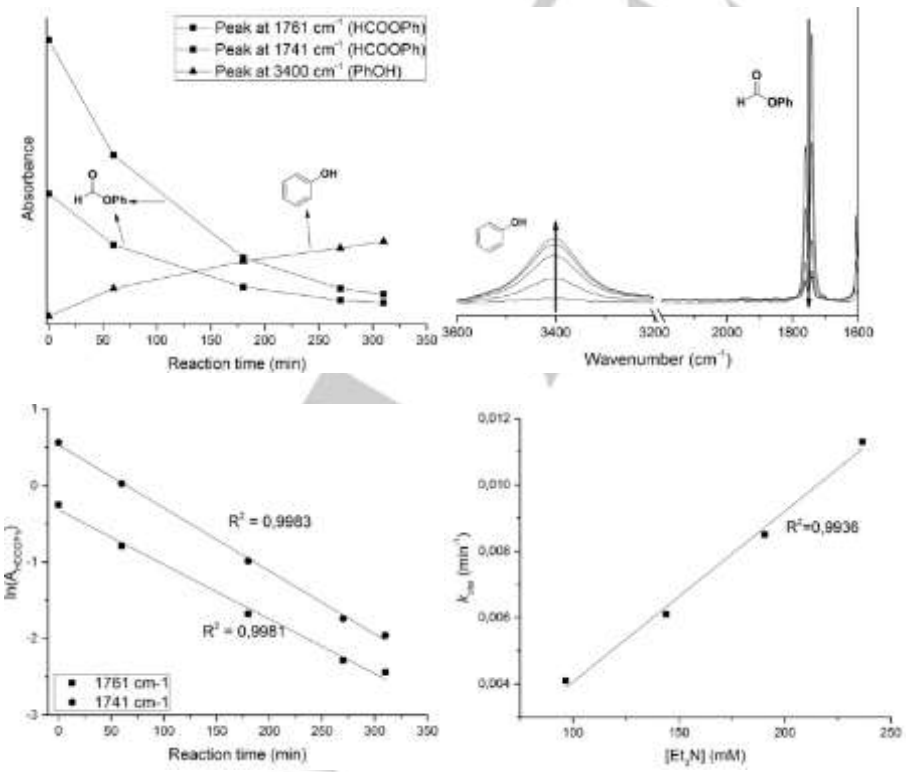
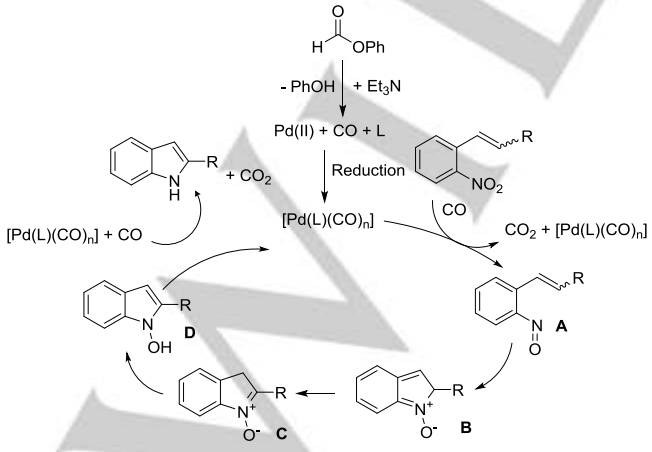


Figure 1. Kinetic analysis of the Et_3N-mediated decarbonylation of phenyl formate (for the experimental procedure see Supporting Information).

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). After 3 h, in the first case complete conversion to CO and phenol was achieved, but no reaction occurred in the latter case. A control experiment carried with HCOOPh alone in CH_3CN, ruled out thermal decarbonylation. In addition, Phen (a relatively basic ligand) was found to be inactive in the same transformation. All these tests support the previously mentioned control experiments (Table S3). To better follow the course of the transformation, 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 and a contemporary increasing of the band at 3400 cm^{-1} due to phenol were detected during the time. Noteworthy, at all stages of the reactions, no other C=O stretching bands were detected. Kinetic studies reveals that the reaction rate is first order in both HCOOPh and Et_3N (Figure 1), 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.

Finally, we devoted our attention to the mechanism of the reductive cyclization. It is generally agreed that nitrosoarenes are active intermediates in the reductive cyclization of nitro compounds using CO as the reductant. The very efficient synthesis of oxazines (Scheme 5) strongly supports the view that nitrosoarenes are intermediately formed even under the present experimental conditions. We were not able to intercept the nitrosoarene derived from **1a** in the same way, but this is due to the high reactivity of nitrosoarenes with olefins[14] and the higher rate of *intra*-molecular reactions with respect to *inter*-molecular ones. Indeed, all previous attempt to obtain *o*-nitrosostyrenes were unsuccessful.[3d, 15]

In the light of the previous experiments, we can propose a mechanism for the described transformations (Scheme 4). Two independent reaction occur: the phenyl formate decarbonylation and the reductive cyclization. Once CO is formed by the Et_3N-mediated decarbonylation reaction, the active Pd species reacts with *o*-nitrostyrene forming the *o*-nitrosostyrene **A**.



Scheme 4. Proposed reaction mechanism.

This readily undergoes *intra*molecular cyclization affording nitronate **B**, which is converted by a 1,5-H-shift to nitronate **C**. The latter is involved in a prototropic equilibrium with the *N*-hydroxyindole **D** that is finally deoxygenated by a second CO equivalent leading to the formation of the desired indole product, regenerating the Pd active species. This mechanism is also supported by experimental[3e] and theoretical evidence.[16]

In conclusion, we have here presented a CO surrogate based efficient, convenient, and general synthetic procedure for the synthesis of nitrogen heterocycles from nitro compounds. In many cases this protocol affords the desired products with selectivities and yields higher than those previously reported using hazardous pressurized CO. In addition, the catalyst (just 1 mol%), the ligand and the CO surrogate are commercially available compounds thus increasing the feasibility of this protocol both on a laboratory and on a larger scale.

Experimental Section

Every manipulation was performed under dinitrogen atmosphere. For a typical reaction conducted with HCOOPh as the CO source, a ~18 mL ACE Pressure Tube was charged with the substrate (0.54 mmol), the appropriate volume of stock solutions of $Pd(CH_3CN)_2Cl_2$ (1 mol%) and Phen (2.5 mol%), HCOOPh (240 µL), Et_3N (40 µL) and the solvent (total liquid amount was 10 mL). Then, the reaction vessel was plugged with a Teflon screwed-cap and immersed in a pre-heated oil bath at 140 °C. 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, GC-MS or subject to column chromatography. For detailed protocols see the Supporting Information.

Acknowledgements

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Keywords: C-H Amination • CO Source • Nitrogen heterocycles • Palladium • Phenyl Formate

[1] For reviews see: a) F. Ragaini, in *Reference Module in Chemistry, Molecular Sciences and Chemical Engineering*, Elsevier, **2016,** DOI: 10.1016/B978-0-12-409547-2.12210-3; b) F. Ragaini, *Dalton Trans.* **2009**, 6251-6266; c) F. Paul, *Coord. Chem. Rev.* **2000**, *203*, 269-323; d) A. M. Tafesh, J. Weiguny, *Chem. Rev.* **1996**, *96*, 2035-2052.

[2] For reviews see: a) F. Ragaini, S. Cenini, E. Gallo, A. Caselli, S. Fantauzzi, *Curr. Org. Chem.* **2006**, *10*, 1479-1510; b) B. C. G. Soderberg, *Curr. Org. Chem.* **2000**, *4*, 727-764; c) S. Cenini, F. Ragaini, *Catalytic Reductive Carbonylation of Organic Nitro Compounds*, Kluwer Academic Publishers, Dordrecht, The Netherlands, **1996**; d) F. Ferretti, D. Formenti, F. Ragaini, *Rend. Lincei* **2017**, *28*, 97-115.

[3] a) F. Ragaini, A. Rapetti, E. Visentin, M. Monzani, A. Caselli, S. Cenini, *J. Org. Chem.* **2006**, *71*, 3748-3753; b) F. Ragaini, F. Ventriglia, M. Hagar, S. Fantauzzi, S. Cenini, *Eur. J. Org. Chem.* **2009**, *2009*, 2185-2189; c) A.

Penoni, K. M. Nicholas, *Chem. Commun.* **2002**, 484-485; d) I. W. Davies, J. H. Smitrovich, R. Sidler, C. Qu, V. Gresham, C. Bazaral, *Tetrahedron* **2005**, *61*, 6425-6437; e) F. Ragaini, P. Sportiello, S. Cenini, *J. Organomet. Chem.* **1999**, *577*, 283-291; f) K. Okuro, J. Gurnham, H. Alper, *J. Org. Chem.* **2011**, *76*, 4715-4720; g) K. Okuro, J. Gurnham, H. Alper, *Tetrahedron Lett.* **2012**, *53*, 620-622; h) N. H. Ansari, C. A. Dacko, N. G. Akhmedov, B. C. G. Söderberg, *J. Org. Chem.* **2016**, *81*, 9337-9349; i) Y. L. Zhang, J. W. Hubbard, N. G. Akhmedov, J. L. Petersen, B. C. G. Soderberg, *J. Org. Chem.* **2015**, *80*, 4783-4790; j) M. Akazome, T. Kondo, Y. Watanabe, *J. Org. Chem.* **1993**, *58*, 310-312; k) D. K. O'Del, K. M. Nicholas, *J. Org. Chem.* **2003**, *68*, 6427-6430; l) B. C. G. Söderberg, J. M. Wallace, J. Tamariz, *Org. Lett.* **2002**, *4*, 1339-1342; m) F. Ragaini, S. Cenini, D. Brignoli, M. Gasperini, E. Gallo, *J. Org. Chem.* **2003**, *68*, 460-466; n) R. S. Srivastava, K. M. Nicholas, *Organometallics* **2005**, *24*, 1563-1568; o) T. H. H. Hsieh, V. M. Dong, *Tetrahedron* **2009**, *65*, 3062-3068; p) M. A. El-Atawy, F. Ferretti, F. Ragaini, *Eur. J. Org. Chem.* **2017**, 1902–1910.; q) F. Ferretti, M. A. El-Atawy, S. Muto, M. Hagar, E. Gallo, F. Ragaini, *Eur. J. Org. Chem.* **2015**, 5712-5715; r) J. H. Smitrovich, I. W. Davies, *Org. Lett.* **2004**, *6*, 533-535; s) S. Tollari, S. Cenini, F. Ragaini, L. Cassar, *J. Chem. Soc., Chem. Comm.* **1994**, 1741-1742; t) F. Ragaini, S. Cenini, E. Borsani, M. Dompe, E. Gallo, M. Moret, *Organometallics* **2001**, *20*, 3390-3398.

[4] a) L. Wu, Q. Liu, R. Jackstell, M. Beller, *Angew. Chem. Int. Ed.* **2014**, *53*, 6310-6320; b) P. Gautam, B. M. Bhanage, *Catal. Sci. Technol.* **2015**, *5*, 4663-4702; c) S. D. Friis, A. T. Lindhardt, T. Skrydstrup, *Acc. Chem. Res.* **2016**, *49*, 594-605; d) H. Konishi, K. Manabe, *Synlett* **2014**, *25*, 1971-1986; e) J. B. Peng, X. X. Qi, X. F. Wu, *Synlett* **2017**, *28*, 175-194; f) J. Cao, Z.-J. Zheng, Z. Xu, L.-W. Xu, *Coord. Chem. Rev.* **2017**, *336*, 43-53. g) V. V. Grushin, H. Alper, *Organometallics* **1993**, *12*, 3846-3850; h) S. N. Gockel, K. L. Hull, *Org. Lett.* **2015**, *17*, 3236-3239.

[5] a) N. Jana, F. Zhou, T. G. Driver, *J. Am. Chem. Soc.* **2015**, *137*, 6738-6741; b) F. Zhou, D.-S. Wang, T. G. Driver, *Adv. Synth. Catal.* **2015**, *357*, 3463-3468.

[6] a) G. Jenner, E. M. Nahmed, H. Leismann, *J. Organomet. Chem.* **1990**, *387*, 315-321; b) G. Jenner, E. M. Nahmed, H. Leismann, *Tetrahedron Lett.* **1989**, *30*, 6501-6502; c) T. Kondo, Y. Tsuji, Y. Watanabe, *Tetrahedron Lett.* **1987**, *28*, 6229-6230.

[7] Indeed, the presence of methyl 2-aminocinnamate was detected only in the case of reactions conducted in the presence of $Ru_3(CO)_{12}$ (alone or in combination with $[Pd(Phen)_2][BF_4]_2$). The ability of Ru to catalyze the reduction of nitro moiety to amine is well known; see for example: F. Ragaini, S. Cenini, M. Gasperini, J. Mol. Catal., A 2001, 174, 51-57.

[8] a) T. Ueda, H. Konishi, K. Manabe, *Org. Lett.* **2012**, *14*, 3100-3103; b) H. Konishi, H. Nagase, K. Manabe, *Chem. Commun.* **2015**, *51*, 1854-1857; c) W. J. Chang, J. F. Li, W. L. Ren, Y. Shi, *Org. Biomol. Chem.* **2016**, *14*, 3047-3052; d) S. P. Chavan, B. M. Bhanage, *Eur. J. Org. Chem.* **2015**, *2015*, 2405-2410; e) Y. Katafuchi, T. Fujihara, T. Iwai, J. Terao, Y. Tsuji, *Adv. Synth. Catal.* **2011**, *353*, 475-482; f) T. Fujihara, T. Hosoki, Y. Katafuchi, T. Iwai, J. Terao, Y. Tsuji, *Chem. Commun.* **2012**, *48*, 8012-8014; g) H. Li, H. Neumann, M. Beller, X.-F. Wu, *Angew. Chem., Int. Ed.* **2014**, *53*, 3183-3186.

[9] a) J.-Y. Mérour, F. Buron, K. Plé, P. Bonnet, S. Routier, *Molecules* **2014**, *19*, 19935; b) J. J. Song, J. T. Reeves, F. Gallou, Z. Tan, N. K. Yee, C. H. Senanayake, *Chem. Soc. Rev.* **2007**, *36*, 1120-1132.

[10] a) W.-L. Jia, Q.-D. Liu, R. Wang, S. Wang, *Organometallics* **2003**, *22*, 4070-4078; b) Q. Liu, L. Thorne, I. Kozin, D. Song, C. Seward, M. D'Iorio, Y. Tao, S. Wang, *J. Chem. Soc., Dalton Trans.* **2002**, 3234-3240.

[11] Reaction conditions for the *n*-butyl formate protocol are those reported in Table S1: 0.27 mmol nitro compound, 1 mol % $[Pd(Phen)_2][BF_4]_2$, 1 mol % $Ru_3(CO)_{12}$, 20 mol % Phen, 2 equiv. Et_3N, 10 mL HCOOnBu, 180 °C, 10 h. Reaction vessel was a ACE Pressure Tube.

[12] C. Crotti, S. Cenini, B. Rindone, S. Tollari, F. Demartin, *J. Chem. Soc., Chem. Comm.* **1986**, 784-786.

[13] S. P. Gorugantula, G. M. Carrero-Martinez, S. W. Dantale, B. C. G. Soderberg, *Tetrahedron* **2010**, *66*, 1800-1805.

[14] L. M. Kogan, *Russ. Chem. Rev.* **1986**, *55*, 1164-1174.

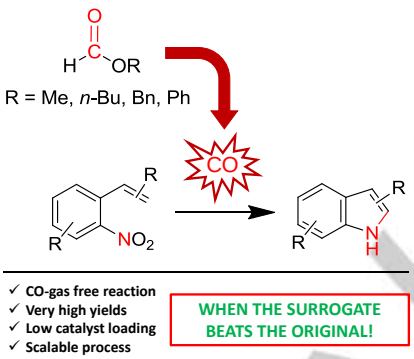
[15] D. Kuzmich, C. Mulrooney, *Synthesis* **2003**, *2003*, 1671-1678.

[16] a) I. W. Davies, V. A. Guner, K. N. Houk, *Org. Lett.* **2004**, *6*, 743-746; b) A. G. Leach, K. N. Houk, I. W. Davies, *Synthesis* **2005**, *2005*, 3463-3467.

Entry for the Table of Contents

COMMUNICATION

A very efficient and general protocol for the preparation of *N*-heterocycles (especially indoles) using phenyl formate as a practical CO surrogate was demonstrated. The desired compounds were obtained in yields often higher than those previously reported using gaseous CO. Mechanistic and kinetic analyses were successfully employed to clarify both the decarbonylation reaction of phenyl formate and the cyclization mechanism.



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