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Palladium Nanoparticles Supported on Smopex-234® as Valuable Catalysts for the Synthesis of Heterocycles

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Abstract: Supported catalysts are important tools for developing green-economy-based processes. Palladium nanoparticles (NPs) that are immobilized on two fibers developed as metal scavengers (i.e., Smopex®-234 and Smopex®-111, 1% *w/w*) have been prepared and tested in copper-free cyclocarbonylative Sonogashira reactions. Their catalytic activity has been compared with that of a homogeneous catalyst (i.e., $PdCl_2(PPh_3)_2$). Pd/Smopex®-234 showed high activity and selectivity in the synthesis of functionalized heterocycles, such as phthalans and isochromans, even when working with a very low amount of palladium (0.2–0.5 mol%). The extension of Pd/Smopex®-234 promoted cyclocarbonylative reactions to propargyl and homopropargyl amides afforded the corresponding isoindoline and dihydrobenzazepine derivatives. A preliminary test on Pd NPs leaching into the solution (1.7×10^{-3} mg) seems to indicate that, at the end of the reaction, almost all of the active metal is present on the fiber surface.

Keywords: palladium nanoparticles; supported catalysts; Sonogashira reactions; carbonylations; phthalan; isochroman; isoindoline; dihydrobenzazepine

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1. Introduction

Recently, the synthesis of heterocycles has received large attention [1,2] due to their increasing importance in the fields of pharmaceutical compounds and industrial chemicals. *N*- and *O*-containing heterocycles are structural motifs frequently found in biologically active compounds.

The 1,3-dihydroisobenzofuran [3,4] (phthalan, Figure 1a) nucleus is present in many natural and synthetic molecules, such as pestacin [5], citalopram [6,7], escitalopram [8–10], talopram [11], and egenine [12,13], which possess antidepressant, antioxidant, antimycotic, antihistaminic, antibacterial and antitumoral properties [5,8,14]. The phthalan derivative FR198248 was found to act as an anti-influenza agent [15,16], carbonylmethyleneisobenzofuran-1-imines have shown promising potential in herbicidal activity [17], and alkylidene functionalized 1,3-dihydroisobenzofurans have recently been tested as luminophores showing good fluorescence properties and remarkable Stokes shifts [18].

Isochroman [19–21] (Figure 1b) is the structural unit of a large number of compounds found in olive oil [22–24], leaves [25], and fungi [26–30]. Many isochromans exhibit anti-inflammatory [31–33], antibacterial [34,35], antifungal [36], antioxidant, and antiplatelet [37,38] activities, while some show cytotoxicity toward human cancer cell lines [39,40] and are used in the treatment of migraine headaches [41]. Moreover, isochroman is the nucleus of the commercial fragrance galaxolide [42–44], which is present in many products, including surface cleaners, laundry products, cosmetics, and perfumes.

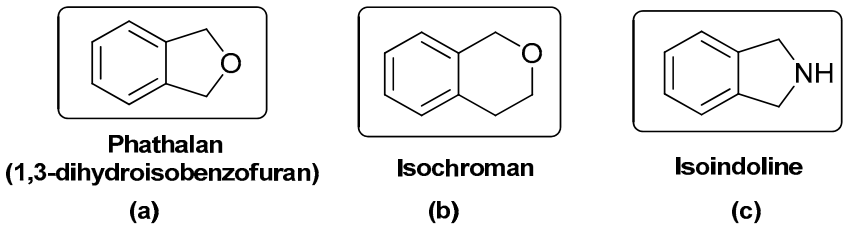


Figure 1. Chemical structure of: (**a**) phthalan; (**b**) isochroman; (**c**) isoindoline.

Nitrogen-containing heterocycles are important substructures that are found in natural and synthetic alkaloids [45,46]. They also serve as an important source of pharmaceuticals and have inspired synthetic chemists to develop novel chemical transformations. For instance, indole [47–49] and its derivatives, such as isoindole [50,51] and isoindoline [52] (Figure 1c), are the basis for compounds possessing relevant biological activities. In particular, isoindoline derivatives are inhibitors of several enzymes involved in numerous diseases, including diabetes, obesity, heart failure, cancer, and mood disorders [53]. Moreover, isoindoline-based ligands are very interesting due to their modular set-up [54]. Finally, isoindoline pigments are particularly relevant, since they cover a wide range of colors from greenish-yellow to red and brown [55].

Owing to their great importance, there has been a continuous interest in developing new and efficient methods for the synthesis of such heterocycles. Several procedures are based on the palladium-promoted cyclization of suitable substrates, such as benzaldehydes [56], benzyl [57–60] and homobenzyl alcohols [61,62], propargyl ethers [63–68], benzylethers [58] and benzylamines [69], anilines [70], propargylamides [71], and arylimides [72].

In this field, Gabriele's group has developed a very interesting methodology based on PdI_2/KI-promoted oxidative cyclization-carbonylation reactions of different substrates affording *O*- and *N*-containing heterocycles [73–82]. Recently, we have described the use of transition-metal-promoted cyclocarbonylative coupling as a valuable tool for the synthesis of polyfunctionalized heterocyclic compounds [83–88].

In all cases described so far, homogeneous organometallic species have been employed as catalysts, thus making its recovery impossible and resulting in the metal contamination of the products. The research of greener methodologies prompted us to investigate the possible use of palladium nanoparticles (Pd NPs) deposited on metal scavengers as catalysts. Commercially available mercapto-functionalized polyolefin fibers, Smopex®-111 and Smopex®-234 (Figure 2), have been chosen as supports; they have been developed for the recovery of platinum group metals (Pt, Pd, Rh) from post-reaction solutions of cross-coupling processes, such as Mizoroki-Heck, Suzuki-Miyaura, and Sonogashira reactions [89–92]. Pd NPs supported on Smopex®-111 and Smopex®-234 were obtained through the metal vapor synthesis (MVS) technique. The versatility and feasibility of this synthetic approach in depositing size-controlled Pd NPs onto a wide range of supports, including organic polymers, have been previously established [93–100].

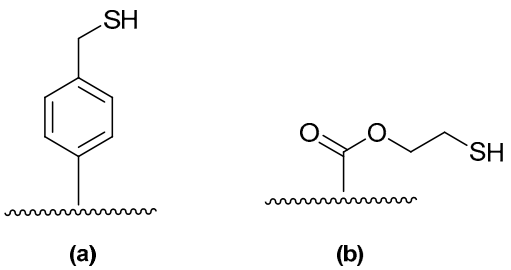


Figure 2. Structure of the supports for the Pd NPs used in this work: (**a**) styril thiol-grafted polyolefin fiber (Smopex®-111); (**b**) mercaptoethyl acrylate-grafted polyolefin fibers (Smopex®- 234).

In the present work, we report that Pd/Smopex®-234 has resulted in an efficient catalyst for the synthesis of phthalan, isochroman, and isoindoline derivatives through cyclocarbonylative Sonogashira reactions. The Pd NPs' dispersion, as well as the nature of the thiol moiety present on the polyolefin fibers, strongly influence the efficiency of the catalytic reactions.

2. Results and Discussion

2.1. Synthesis and Morphology of the Catalysts

Palladium NPs were obtained according to the MVS technique (Figure 3). This approach allowed for the generation of Pd nanoclusters that were weakly stabilized by organic solvents, which were then dispersed on Smopex®-111 and Smopex®-234 supports, respectively, by simple impregnation at 25 °C. Further reduction or thermal treatments of the catalysts were not required.

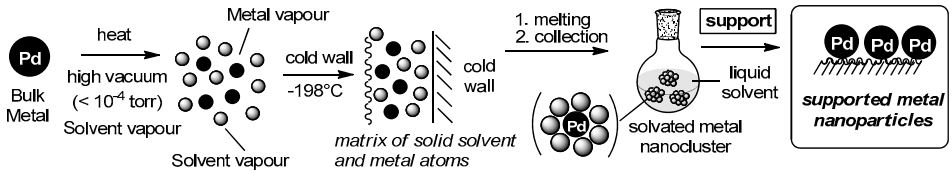


Figure 3. Schematic representation of the MVS approach to obtain supported Pd NPs.

More in detail, Palladium vapors were co-condensed at a low temperature (77 K) with vapors of weakly stabilizing organic ligands (i.e., a mixture of mesitylene and 1-hexene) using a commercially available glass reactor. Upon warming, the frozen matrix melted and the nucleation and growth processes of the metal particles occurred, affording metal nanoclusters that were weakly stabilized by the solvent molecules, called solvated metal atoms (SMAs). The interaction of the metal vapors with the solvent matrix very quickly quenched the kinetic energy of metal atoms. The final sizes of the metal aggregates were greatly influenced by the solvent employed and the amount used, allowing for good control over their size. The Pd-SMA was handled at a low temperature (between 223 and 243 K) under an inert atmosphere, and it was used as a precursor for the preparation of supported Pd nanoparticles by simply mixing the SMA with the solid supports (i.e., Pd/Smopex®-234 and Pd/Smopex®-111) at room temperature. The metal quickly separated quantitatively from the solvent by interacting with the support surface, thus affording solid catalytic systems without the need for poisons (i.e., halide from metal salt precursors in catalysts prepared through reduction methods). One of the main advantages of the MVS approach is that it allows for the preparation of supported catalytic systems where the metal is deposited directly in its reduced form, so that the calcination and activation processes of the conventional wet deposition method are not required.

The morphology of Pd/Smopex®-111 and Pd/Smopex®-234 was investigated through transmission electron microscopy (TEM). Representative images of both systems are reported in Figure 4. The two systems exhibited different structural features, pointing out the crucial role of the organic support in controlling the final dispersion of the metal phase. Quite a low level of dispersion of Pd NPs was observed when supported on Smopex®-111. The presence of large agglomerates of roundish NPs, having diameters that were less than 10 nm in size (d_m = 3.5 nm), was detected (Figure 4a).

On the other hand, the analysis of Pd/Smopex®-234 revealed the great affinity of this support for the as-prepared MVS-derived Pd NPs (Figure 4b), which prevents further NP aggregation phenomena during their immobilization. Indeed, a highly homogeneous dispersion of small Pd NPs (d_m = 1.5 nm), which densely populated the surface of the organic fiber, was detected. Indeed, the mercaptoethyl acrylate group of Smopex®-234 is able to chelate the Pd NPs much better than the thiol functional group of Smopex®-111. Therefore, on Smopex®-234 Pd NPs are highly dispersed and stabilized. Moreover, assuming that the Pd NPs were spherical in shape, the theoretical exposed Pd fraction and

metal-specific surface areas (SSAs) for both catalysts were calculated from HRTEM data through applying the following Equation (1):

$$d_{VS}/d_{at} = 3.32/(FE)^{1.23} \quad (1)$$

where d_{VS} is the size of Pd crystallites, d_{at} is the atomic diameter of Pd (i.e., 0.275 nm), and FE is the exposed fraction of Pd [101], and Equation (2):

$$SSA = 3\,\Sigma n_i r_i^2/(\Sigma \rho_{Pd} \Sigma n_i r_i^3)\ m^2/g \quad (2)$$

where r_i is the mean radius of the size class containing n_i particles, and ρ_{Pd} is the volumetric mass of Pd (12.02 g/cm^3). As a result, Pd/Smopex®-234 exhibited a dispersion of 67% and an SSA = 116 m^2/g, whereas Pd/Smopex®-111 exhibited a dispersion of 33% and an SSA = 48 m^2/g.

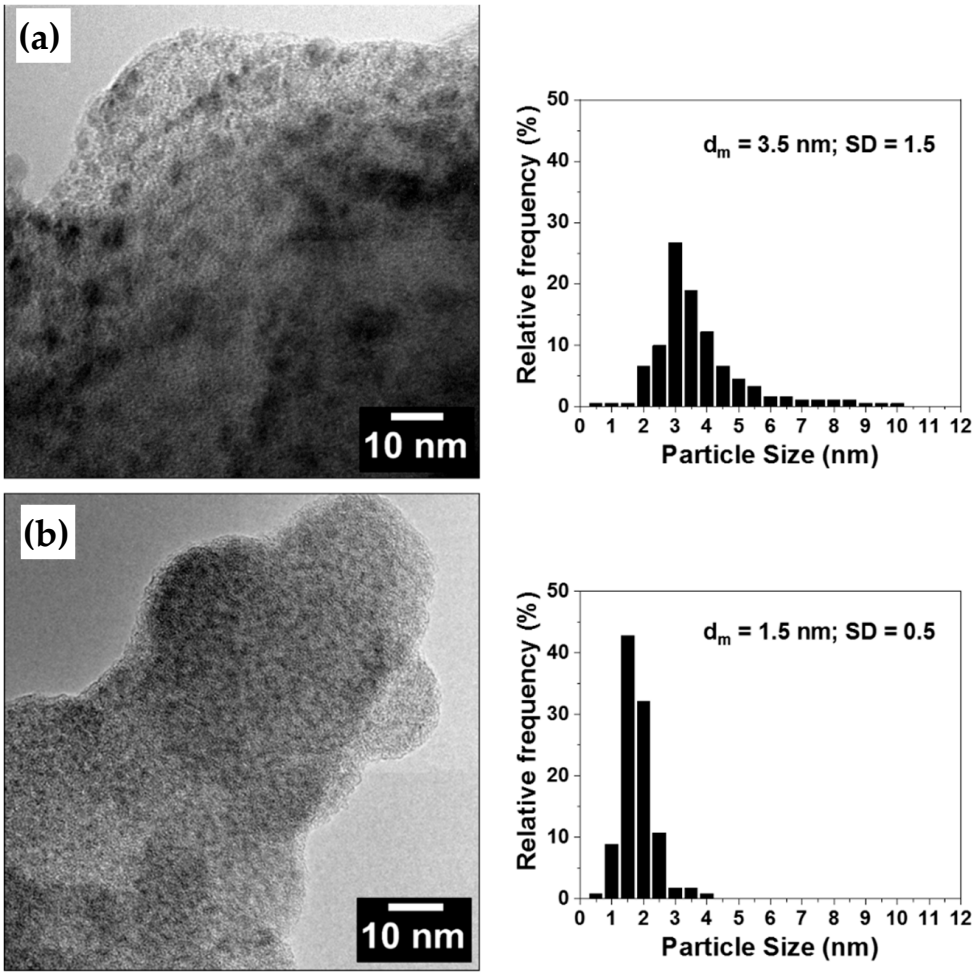


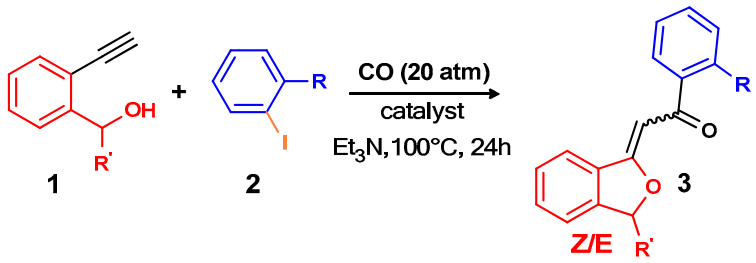
Figure 4. Representative TEM micrograph and histogram of the particle size distribution of Pd/Smopex®-111 (**a**) and Pd/Smopex®-234 (**b**).

2.2. Catalytic Activity of Pd/Smopex®-111 and Pd/Smopex®-234

First of all, the supported catalytic systems Pd/Smopex®-111 and Pd/Smopex®-234 were tested in the coupling between 2-ethynylbenzyl alcohol **1a** and iodobenzene **2a,** which were chosen as model compounds. The catalytic performance of the supported Pd NPs was compared with the activity of the $PdCl_2(PPh_3)_2$ used as a homogenous reference catalyst. The reactions were performed in Et_3N, which was used as a base and as a solvent, in a stainless-steel autoclave that was pressurized to 20 atm of carbon monoxide. While

palladium nanoparticles that were supported on Smopex®-111 were totally inactive (Table 1, entry 2), those deposited on the Smopex®-234 fiber showed high catalytic efficiency in promoting the synthesis of phthalan derivative **3aa** quantitatively, even in the presence of a very low amount of catalyst (0.2 mol%).

Table 1. Palladium-promoted synthesis of phthalans via cyclocarbonylative Sonogashira reactions.



Entry [1]	1	R′	2	R	Catalyst [2]	Pd Loading (mol%)	Conversion (%) [3]	3	Selectivity (%) [3,4]	
									(*Z*)	(*E*)
1	a	H	a	H	$PdCl_2(PPh_3)_2$	0.2	100	aa	65 (68)	35 (25)
2	a	H	a	H	Pd/Smopex®-111	0.2	0	aa	/	/
3	a	H	a	H	Pd/Smopex®-234	0.2	100	aa	75	25
4	a	H	b	*o*-Me	Pd/Smopex®-234	0.2	100	ab	79 (70)	21 (18)
5	a	H	c	*o*-CN	Pd/Smopex®-234	0.2	100	ac	100 (82)	/
6	b	*t*-Bu	a	H	$PdCl_2(PPh_3)_2$	0.2	28	ba	22	78
7	b	*t*-Bu	a	H	$PdCl_2(PPh_3)_2$	0.5	100	ba	24 (15)	76 (57)
8	b	*t*-Bu	a	H	Pd/Smopex®-234	0.2	16	ba	22	78
9	b	*t*-Bu	a	H	Pd/Smopex®-234	1	82	ba	21	79

[1] The reactions were performed with *ortho*-ethynylbenzyl alcohol **1** (2 mmol) and iodoarene **2** (2 mmol), in Et_3N (5 mL) under CO atmosphere (20 atm), at 100 °C for 24 h. [2] Supported catalysts contain 1% *w/w* of palladium. [3] Conversion and selectivity were determined by ^{1}H-NMR analysis. [4] In parentheses, the yields of pure products are reported.

The unexpected difference observed in the catalytic activity of the Pd NPs deposited on the two Smopex® fibers (Table 1, entry 2 vs. entry 3) could be firstly related to the different morphological features of the two species (i.e., small particles well-dispersed for Pd/Smopex®-234 and the presence of large aggregates in the case of Pd/Smopex®-111). Moreover, a hypothetical mechanism of action of Pd/Smopex®-234 catalyst has been added in the Supplementary Materials.

The behavior of Pd/Smopex®-234 was also compared with that of homogeneous $PdCl_2(PPh_3)_2$ (Table 1, entry 1 vs. entry 3): the reaction promoted by Pd NPs supported on Smopex®-234 took place with higher stereoselectivity toward the more stable isomer [102,103] (Z)-**3aa** (75%) with respect to the reaction carried out with the homogeneous catalyst (65%). The increase of the (Z) isomer amount after purification (i.e., silica column chromatography) may be due to the interconversion of (E) stereoisomer into the (Z) one, as already reported in the literature [104]. Indeed, as can be verified in the ^{1}H-NMR of the crude product (see Supplementary Materials) the composition of the two isomers changes after purification, probably due to traces of acid.

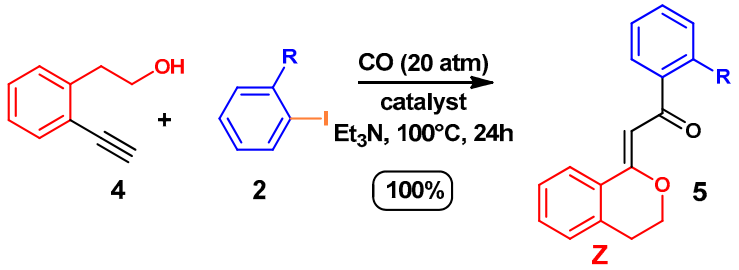
The observed catalytic trend was confirmed by the reactions carried out using functionalized iodoarenes **2b** and **2c** (Table 1, entries 4–5), which possess different stereo-electronic features. Pd/Smopex®-234 was able to catalyze the cyclocarbonylative reactions quantitatively, affording the corresponding phthalans, (Z)-**3ab** and (Z)-**3ac**, in high yields (70–82%) after purification. Moreover, in the case of nitrile derivative **3ac**, a complete stereoselectivity towards the (Z) isomer was observed.

The catalytic activity of Pd/Smopex®-234 was subsequently tested in the reaction of t-butylbenzyl alcohol **1b** with iodobenzene **2a** (Table 1, entries 8–9). The stereoselectivity of the process favored the formation of the (E) isomer in all the reactions ((Z)/(E) ratio of about 20/80), probably due to the steric hindrance of benzyl alcohol **1b**. The same factor could be

the reason for the overall reduced rate of the catalytic cycle. Indeed, in the cases of both $PdCl_2(PPh_3)_2$- and Pd/Smopex®-234-promoted reactions, a substrate conversion of almost 20% was observed when a 0.2 mol% of palladium was used. (Table 1, entries 6 and 8). An increase of the catalytic amount to 0.5 mol% for the homogeneous complex determined a quantitative formation of phthalan **3ba** (Table 1, entry 7). Analogously, an 82% conversion was observed when 1 mol% of Pd/Smopex®-234 was used (Table 1, entry 9).

Prompted by the good results obtained in the synthesis of phthalans **3** promoted by Pd/Smopex®-234 cyclocarbonylative Sonogashira reactions, we extended our investigation to the reaction of 2-(2-ethynylphenyl)ethanol **4** with iodoarenes **1a-c** (Table 2), which was performed in the presence of homogeneous $PdCl_2(PPh_3)_2$ and supported Pd/Smopex®-234 catalysts. In all cases, the reactions showed a complete conversion of the precursors and the exclusive formation of the (Z) stereoisomer of isochromans **6a-c**, which were isolated as pure products in very high yields (90–95%). To our delight, a very low amount of Pd/Smopex®-234 (0.2 mol%) was able to catalyze the cyclocarbonylative reactions with complete chemo- and stereoselectivity.

Table 2. Palladium-promoted synthesis of isochromans via cyclocarbonylative Sonogashira reactions.



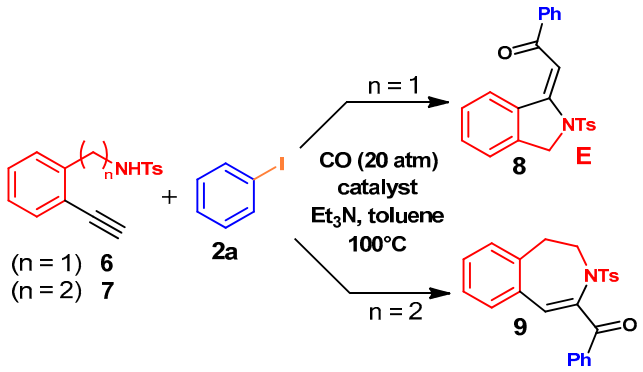
Entry [1]	R	2	Catalyst [2]	Yield (%) [3]	R	5
1	H	a	$PdCl_2(PPh_3)_2$	90	H	a
2	H	a	Pd/Smopex®-234	93	H	a
3	*o*-Me	b	Pd/Smopex®-234	95	*o*-Me	b
4	*o*-CN	c	Pd/Smopex®-234	91	*o*-CN	c

[1] The reactions were performed with *ortho*-ethynylhomobenzyl alcohol **4** (2 mmol) and iodoarene **2** (2 mmol), in Et_3N (5 mL), under CO atmosphere (20 atm), and in the presence of 0.2 mol% of Pd, at 100° for 24 h. [2] Pd/Smopex®-234 contains 1% *w/w* of palladium. [3] The yields of pure products are reported.

Finally, the protocol based on Pd/Smopex®-234 cyclocarbonylative reactions was applied to the preparation of nitrogen-containing heterocycles. For this purpose, *ortho*-ethynylbenzyl tosylamide **6** and *ortho*-ethynylhomobenzyl tosylamide **7** were chosen as model compounds and tested in the reaction with iodobenzene **2a** (Table 3). First of all, 0.2 mol% of homogeneous $PdCl_2(PPh_3)_2$ (Table 3, entry 1) and supported Pd/Smopex®-234 (Table 3, entry 2) were employed in the reaction of tosylamide **6** with **2a**, under the same experimental conditions (for 4 h at 100 °C, under 20 atm of CO, in Et_3N, and using toluene as solvents). A relevant reduction of the reaction rate was detected when cyclocarbonylation was carried out with Pd NPs supported on Smopex®-234. Nevertheless, (*E*)-1-phenyl-2-(2-tosylisoindolin-1-ylidene) ethanone **8** was obtained as an exclusive product. In order to improve the conversion of the process, the reaction was repeated with 0.4 mol% of Pd/Smopex®-234 for a longer reaction time (24 h); under these experimental conditions, the quantitative formation of isoindoline derivative **8** was finally achieved (Table 3, entry 4).

The Pd/Smopex®-234 catalyst was subsequently applied to the cyclocarbonylative Sonogashira reaction between tosylamide **7** and iodobenzene **2a**. The reaction took place with 0.4 mol% of supported Pd NPs and solely yielded dihydrobenzazepine **9**, which is an important nucleus of many biologically active natural products and pharmaceutical compounds [105,106].

Table 3. Palladium-promoted synthesis of *N*-heterocyclic compounds via cyclocarbonylative Sonogashira reactions.



Entry [1]	n	Tosylamide	Catalyst [2]	Pd Loading (mol%)	Reaction Time (h)	Conversion (%) [3]	Product [4]
1	1	**6**	$PdCl_2(PPh_3)_2$	0.2	4	100	**8** (75%)
2	1	**6**	Pd/Smopex®-234	0.2	4	18	**8**
3	1	**6**	Pd/Smopex®-234	0.2	24	69	**8**
4	1	**6**	Pd/Smopex®-234	0.4	24	100	**8**
5	2	**7**	Pd/Smopex®-234	0.4	24	92	**9** (63%) [5]

[1] The reactions were performed with tosylamide **6** or **7** (2 mmol) and iodobenzene **2a** (2.5 mmol), in Et_3N (3 mL) and toluene (2 mL), under CO atmosphere (20 atm), at 100 °C. [2] Pd/Smopex®-234 contains 1% *w/w* of palladium. [3] Conversion was estimated through the ^{1}H-NMR analysis of crude products. [4] The yields of pure products are reported in parentheses. [5] Dihydrobenzazepine **9** was obtained as a mixture of two conformers: *s*-trans/*s*-cis (60/40 molar ratio).

Finally, preliminary tests of Palladium leaching and catalyst recovery at the end of the reaction were carried out. With this aim, the autoclave was charged with iodobenzene **2a** (0.6 mmol), tosylamide **6** (0.5 mmol), Et_3N (1.5 mL), toluene (1.0 mL), and Pd/Smopex®-234 (0.4 mol% of Pd). After 24 h at 100 °C, the CO pressure was discharged (under fume hood), and the hot reaction mixture was filtered (using a Teflon filter, 0.2 mm) under nitrogen atmosphere. The palladium content in the resulting solution was determined by ICP-OES analysis and was found to be 0.8 *w/w*% of the initial Pd (i.e., 1.7×10^{-3} mg). This very low value will prompt us to carry out further experiments, such as recycling of the catalyst and Maitlis hot filtration tests [107,108], to evaluate the mechanism (homogeneous or heterogeneous) of the Pd/Smopex®-234 catalyst in the cyclocarbonylative Sonogashira reaction.

3. Materials and Methods

3.1. Preparation of Solvated Palladium Atoms Solutions

Palladium vapors were generated under reduced pressure (10^{-5} mBar) through the resistive heating of 500 mg of the metal in an alumina-coated tungsten crucible; they were then co-condensed at liquid N_2 temperature (−195 °C) with vapors of 1-hexene (30 mL) and mesitylene (30 mL) in a glass reactor [109]. The reactor chamber was heated to the melting point of the solid matrix (−40 °C), and the resulting brown solution (called Pd-SMA) was siphoned and handled at a low temperature (about −40 °C). The palladium content of the obtained Pd-SMA, determined through an ICP-OES analysis, was 2.3 mg of Pd/mL.

3.2. Preparation of Supported Palladium Catalysts

In a Schlenk tube, Pd-SMA (27 mL, 62.1 mg of Palladium) was added to a suspension of the support (Smopex®-111 or Smopex®-234) (6.2 g) in mesitylene (20 mL). The resulting mixture was stirred for 6 h at 25 °C. The colorless solution was then removed, and the light-brown solid was washed with *n*-pentane (3 × 20 mL) and dried under reduced pressure. The metal content of Pd/Smopex®-111 and Pd/Smopex®-234 (i.e., 1% *w/w*) was confirmed through ICP-OES analysis.

3.3. Synthesis of Phthalans: General Procedure

In a typical run (see Table 1), *ortho*-ethynylbenzyl alcohol **1** (2.0 mmol), iodoarene **2** (2.0 mmol), and Et_3N (5 mL) were mixed, under CO atmosphere, into a Schlenk tube. This solution was siphoned in a 25 mL stainless steel autoclave, previously charged with the Pd catalyst (0.2–1 mol%), and placed under vacuum (0.1 Torr). The reactor was pressurized with carbon monoxide (20 atm), and the resulting mixture was stirred at 100 °C for 24 h. After the removal of excess CO (under fume hood), the reaction mixture was diluted with CH_2Cl_2 (20 mL), washed with brine (20 mL), dried over anhydrous Na_2SO_4, and the solvent was removed under reduced pressure. Reagent conversion and product composition were determined through ^{1}H-NMR analysis. Crude products were purified through column chromatography on silica gel and were characterized by ^{1}H-NMR and ^{13}C-NMR techniques.

3.4. Synthesis of Isochromans: General Procedure

In a typical run (see Table 2), 2-(2-ethynylphenyl)ethanol **4** (2.0 mmol), iodoarene **2** (2.0 mmol), and Et_3N (5 mL) were mixed, under CO atmosphere, into a Schlenk tube. This solution was siphoned in a 25 mL stainless steel autoclave, previously charged with the Pd catalyst (0.2 mol%), and placed under vacuum (0.1 Torr). The reactor was pressurized with carbon monoxide (20 atm), and the resulting mixture was stirred at 100 °C for 24 h. After the removal of excess CO (under fume hood), the reaction mixture was diluted with CH_2Cl_2 (20 mL), washed with brine (20 mL), dried over anhydrous Na_2SO_4, and the solvent was removed under reduced pressure. Reagent conversion and product composition were determined through ^{1}H-NMR analysis. Crude products were purified through column chromatography on silica gel and were characterized by ^{1}H-NMR and ^{13}C-NMR techniques.

3.5. Synthesis of N-Heterocyclic Compounds: General Procedure

In a typical run (see Table 3), *ortho*-ethynyl(homo)benzyl tosylamide **6** or **7** (2.0 mmol), iodobenzene **2a** (2.5 mmol), Et_3N (3 mL), and toluene (2 mL) were mixed, under CO atmosphere, into a Schlenk tube. This solution was siphoned in a 25 mL stainless steel autoclave, previously charged with the Pd catalyst (0.2–0.4 mol%), and placed under vacuum (0.1 Torr). The reactor was pressurized with carbon monoxide (20 atm), and the resulting mixture was stirred at 100 °C for a selected time (4–24 h). After the removal of excess CO (under fume hood), the reaction mixture was diluted with CH_2Cl_2 (20 mL), washed with brine (20 mL), dried over anhydrous Na_2SO_4, and the solvent was removed under reduced pressure. Reagent conversion and product composition were determined through ^{1}H-NMR analysis. Crude products were purified through column chromatography on silica gel or neutral alumina and were characterized through ^{1}H-NMR and ^{13}C-NMR techniques.

4. Conclusions

In conclusion, we have reported that Pd NPs, prepared according to the MVS technique, can be easily deposited on commercial thiol-based metal scavengers Smopex®-111 and Smopex®-234, affording Pd/Smopex®-111 and Pd/Smopex®-234 systems. The latter material exhibits a very high homogeneous dispersion of small Pd NPs (d_m = 1.5 nm) without the presence of Pd NP aggregates, as observed for Pd/Smopex®-111. Both systems were initially studied as supported catalysts in the cyclocarbonylative reaction of 2-ethynylbenzyl alcohol with iodoarenes to generate phthalans. Pd/Smopex®-234 showed a catalytic efficiency comparable to that observed with the $PdCl_2(PPh_3)_2$ organometallic complex, which was used as a reference homogeneous catalyst. On the other hand, Pd/Smopex®-111 was completely unable to promote the reaction. Pd/Smopex®-234 also proved to be very efficient in the synthesis of isochroman, isoindoline, and dihydrobenzazepine derivatives with high chemo- and stereoselectivity.

Almost all the cyclocarbonylative Sonogashira reactions were carried out with a very small amount of catalyst (0.2–0.4 mol% of Pd) in both phosphine-free and Cu-free

conditions, thus enhancing the potentialities of Pd/Smopex®-234 as a promising catalyst for heterocycle synthesis.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/catal11060706/s1: additional experimental details; supplementary figures; ^{1}H-NMR and ^{13}C-NMR spectra of the pure products of cyclocarbonylative reactions.

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