

# A Palladium Tetraiodide Supported Catalyst for the Oxidative Carbonylation of $\beta$ -Amino Alcohols to 2-Oxazolidinones

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A novel PdI<sub>4</sub><sup>2-</sup>-supported catalyst, based on imidazolium-functionalized polyhedral oligomeric silsesquioxanes (POSS) functionalized with imidazolium arms grafted on amorphous silica, is prepared through a straightforward synthetic procedure allowing to accede to high local concentration spots of palladium sites surrounding the POSS core. The hybrid material was fully characterized by thermogravimetric analysis coupled with differential scanning calorimetry (TGA–DSC), transmission electron microscopy (TEM), inductively coupled plasma optical emission spectroscopy (ICP–OES), and X-ray photoelectron spectroscopy (XPS). This material was successfully used as heterogeneous catalyst for the oxidative carbonylation of  $\beta$ -amino

alcohols to 2-oxazolidinones as well as 2-aminopyridin-3-ol to oxazolo[4,5-*b*]pyridin-2(3*H*)-one under relatively mild conditions (100 °C for 3 h under 40 atm of a 4:1 mixture CO–air) in DME as the solvent and with aerobic oxygen as the simplest external oxidant, with the formation of water as benign coproduct. The catalyst could be successfully recycled up to four times, before beginning to undergo partial deactivation due to palladium reduction, as evidenced by XPS and TEM. ICP–OES analysis of some representative products evidenced a low metal contamination (palladium content <1 ppm), making our approach interesting for applications in the life science field, where a high degree of purity is required.

## 1. Introduction

2-Oxazolidinones are an important class of heterocyclic compounds, which present a wide range of biological activities,<sup>[1]</sup> including antimicrobial<sup>[2]</sup> and anticancer<sup>[3]</sup> properties. Moreover,

nonracemic oxazolidinones are widely used as chiral auxiliaries for enantioselective syntheses.<sup>[4]</sup> A useful approach for the synthesis of 2-oxazolidinones is represented by oxidative carbonylation of readily available  $\beta$ -amino alcohols, using carbon monoxide as the simplest carbonyl source.<sup>[5]</sup> In particular, the PdI<sub>2</sub>/KI-catalyzed process is carried out using as external oxidant the simplest and most available oxidant, namely, oxygen from air, with formation of water as benign co-product.<sup>[6]</sup> This reaction was carried out by our research group several years ago,<sup>[6b]</sup> and is efficient when carried out in 1,2-dimethoxyethane as solvent under homogeneous conditions (the catalytically active species PdI<sub>4</sub><sup>2-</sup> being formed in situ under the reaction conditions from PdI<sub>2</sub> and the excess KI).<sup>[6]</sup> Mechanistically, as shown in Scheme 1, the process takes place through the formation of a carbamoyl-palladium intermediate (from the reaction between the amino group of the substrate, PdI<sub>2</sub> and CO), which then undergoes intramolecular nucleophilic displacement by the hydroxyl group (Scheme 1, anionic iodide ligands are omitted for clarity).

Considering the importance of synthesizing 2-oxazolidinones with low level of metal contamination, as required for pharmacological applications,<sup>[7]</sup> in this work we have studied the possibility to develop a new PdI<sub>4</sub><sup>2-</sup>-based heterogeneous catalyst able to promote the oxidative carbonylation of  $\beta$ -amino alcohols with a low degree of palladium contamination into the final product.

## 2. Results and Discussion

Recently, we reported the first example of a PdI<sub>4</sub><sup>2-</sup>-based heterogeneous catalyst, which was prepared in two steps

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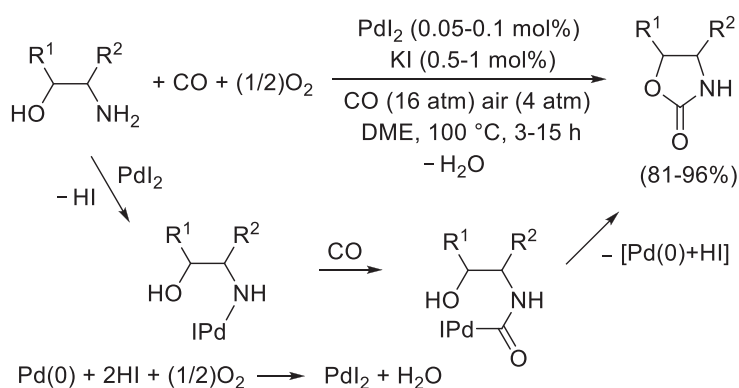
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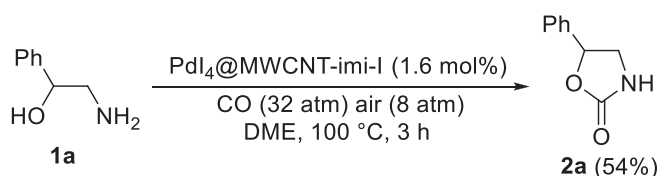
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Supporting information for this article is available on the WWW under  
<https://doi.org/10.1002/cctc.202401841>

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Scheme 1. Pd<sub>2</sub>/KI-catalyzed oxidative carbonylation of β-amino alcohols to oxazolidinones.<sup>[6]</sup>



Scheme 2. Oxidative carbonylation of 2-amino-1-phenylethan-1-ol (**1a**) with heterogeneous catalyst Pd<sub>4</sub>@MWCNT-imi-I.

using ionic liquid-functionalized multiwalled carbon nanotubes (Pd<sub>4</sub>@MWCNT-imi-I).<sup>[8]</sup> This catalyst proved efficient for the oxidative monoaminocarbonylation of terminal alkynes to 2-ynamides, carried out in dioxane as the solvent. Accordingly, we firstly tried to use this material for catalyzing the oxidative carbonylation of a model β-amino alcohol substrate, namely, 2-amino-1-phenylethan-1-ol (**1a**) to afford 5-phenyloxazolidin-2-one (**2a**) under heterogeneous conditions. When **1a** was allowed to react in 1,2-dimethoxyethane (DME, 0.30 mmol of **2a** per mL of DME) with CO (32 atm) and O<sub>2</sub> (from air, 8 atm)<sup>[9]</sup> in the presence of 1.6 mol% of Pd<sub>4</sub>@MWCNT-imi-I catalyst at 100 °C for 3 h, **2a** was obtained in 54% isolated yield (Scheme 2).

To assess the possibility of improving this result, we attempted to immobilize Pd<sub>4</sub><sup>2+</sup> on a different imidazolium-based hybrid material in order to obtain a more efficient heterogeneous catalyst for this process. Thus, commercially available amorphous silica was modified with imidazolium-functionalized polyhedral oligomeric silsesquioxane (POSS-imi) units, according to a previously developed synthetic method.<sup>[10]</sup> Reaction of octakis(3-iodopropyl)-octasilsesquioxane (**3**) with triethoxy-3-(2-imidazolyl)propylsilane in refluxing toluene followed by treatment with amorphous silica for 72 h afforded grafted silica **4**. The latter was allowed to react with an excess of 1-methylimidazole in refluxing toluene for 72 h to yield a new hybrid material, SiO<sub>2</sub>-POSS-imi-I (**5**), which was treated with a solution of K<sub>2</sub>Pd<sub>4</sub> in acetonitrile, in the dark, to give Pd@SiO<sub>2</sub>-POSS-imi-I (**6**) by an anionic metathesis reaction (Scheme 3).

Pd@SiO<sub>2</sub>-POSS-imi-I material (**6**) was characterized by thermogravimetric analysis coupled with differential scanning calorimetry (TGA–DSC) under air flow (Figure 1). The TGA profile of **6** indicates a good thermal stability of the material, which showed no weight loss up to 250 °C. Above temper-

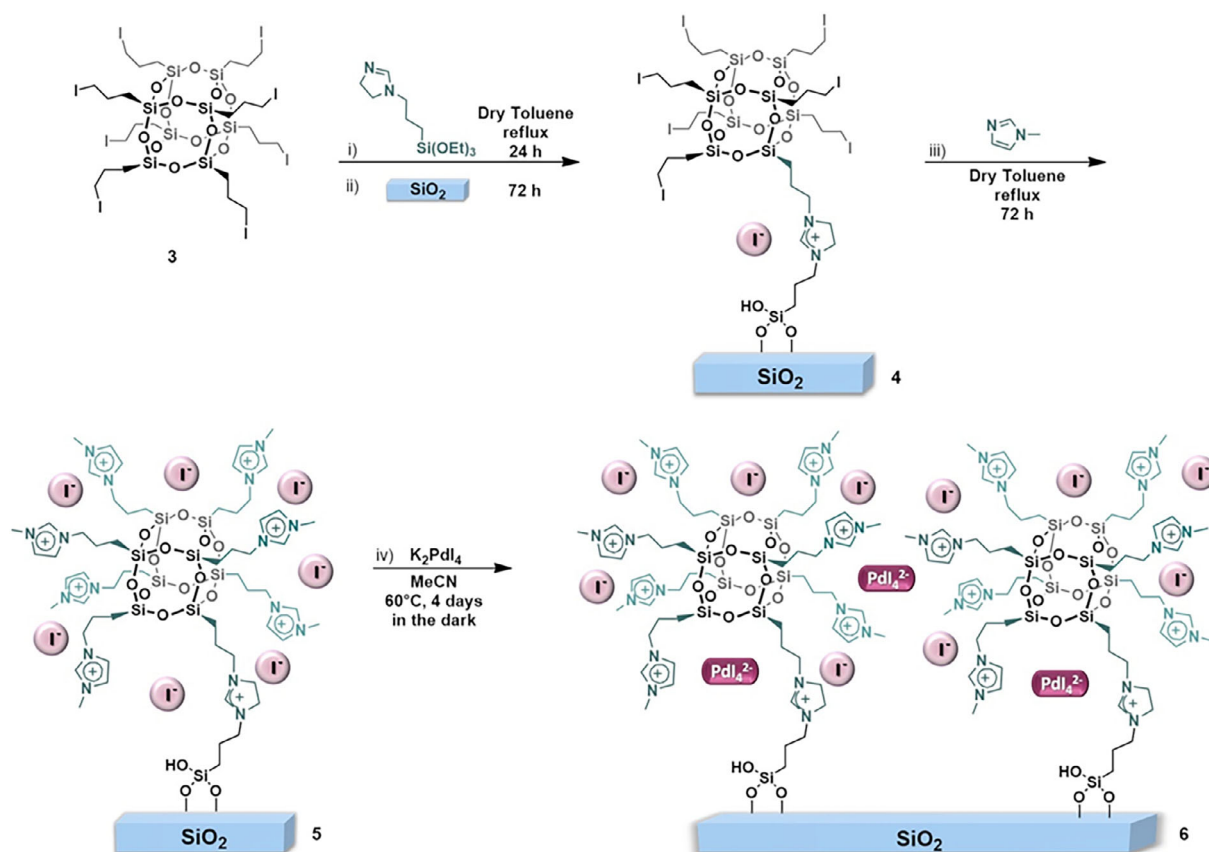
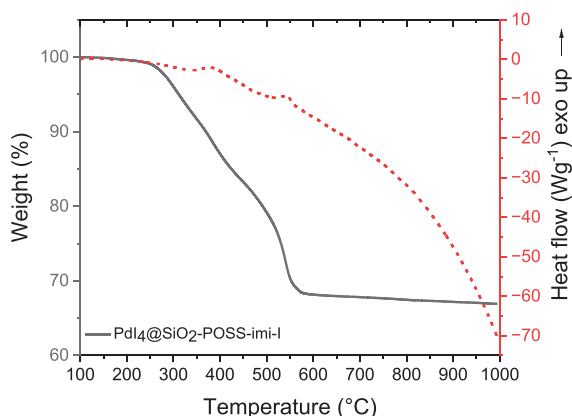
atures 250–600 °C, a weight loss (~30% w/w), associated by DSC to exothermic processes, can be ascribed to the complete burning of the organic functionalities. Palladium loading of **6** was quantified by inductively coupled plasma optical emission spectroscopy (ICP–OES) and was found to be 2.59 wt%.

XPS analysis was used to collect information about the surface composition of **6** and to evaluate the oxidation state of the supported palladium species. Figure 2 shows (a) the survey spectrum as well as (b) the high-resolution XPS of the Pd3d region of the catalyst. The first spectrum (a) shows the characteristic peaks for all the expected atomic species, whereas the second spectrum (b) shows the spin-orbit coupling Pd3d<sub>5/2</sub> and Pd3d<sub>3/2</sub> at 336.9 and 342.3 eV, respectively, indicating that in the material Pd(II) is the only palladium species present.<sup>[11]</sup>

Material **6** was further analyzed by means of transmission electron microscopy (TEM) with the aim to collect morphological information (Figure 3). Nevertheless, due to the amorphous nature of the silica used as support, TEM pictures did not reveal any appreciable features, although the presence of Pd nanoparticles can be excluded in the fresh material.

The newly developed Pd<sub>4</sub><sup>2+</sup>-based heterogeneous catalyst **6** was then tested in the oxidative carbonylation of **1a** under the same conditions previously used with Pd<sub>4</sub>@MWCNT-imi-I. With 1.6 mol% catalyst, in DME (0.30 mmol of **1a** per mol of DME) at 100 °C for 3 h under 32 atm of CO and 8 atm of air, **2a** was obtained in 77% isolated yield (Scheme 4). Thus, this catalyst proved more active with respect to Pd<sub>4</sub>@MWCNT-imi-I (**2a** yield was 54%; see Scheme 2). This result is seen because the silica-based hybrid material has a specific surface area (SSA) of about 280 m<sup>2</sup>/g<sup>[10]</sup> and all the imidazolium moieties, and subsequently all the catalytically active Pd<sub>4</sub><sup>2+</sup> species, are grafted only onto the external and accessible surface of silica. On the other hand, in Pd<sub>4</sub>@MWCNT-imi-I, the poly-imidazolium network surrounding the nanotubes is rather thick and tetraiodopalladate species are distributed in a larger and less accessible volume in a material with a very low SSA, <20 m<sup>2</sup>/g (see for instance some previous examples).<sup>[11]</sup>

Catalyst **6** could be easily recovered by filtration and reused up to three times without appreciable loss of activity (**2a** yields were 78%, 79%, and 74%). Partial catalyst deactivation, however, began to occur starting from the fourth recycle (**2a** yield was

Scheme 3. Synthesis of Pd<sub>4</sub>@SiO<sub>2</sub>-POSS-imi-I (6).Figure 1. TGA–DSC analyses of Pd<sub>4</sub>@SiO<sub>2</sub>-POSS-imi-I (6) recorded under airflow (10 °C/min).

55% after the fourth recycle and dropped to 31% after the fifth recycle; see Scheme 4). In any case, a limited palladium leaching occurred under these conditions. In fact, ICP analysis of the reused catalyst revealed that more than 95% of palladium was still present in the solid material even after the fifth recycle.

We also characterized the catalyst after the fifth recycle by XPS and TEM (Figure 4). The high-resolution XPS of the Pd3d region reveals that during the reactions the palladium in the recovered material from the reaction mixture is partially reduced (60% of Pd(II) and 40% of Pd(0)). Hence, the presence of such

unreactive Pd(0) species (Pd3d5/2 binding energy = 335.1 eV) may be responsible for the decreased catalytic activity. TEM picture of the recycled catalyst (Figure 4b), compared with the fresh material reported in Figure 3, displays a darker appearance of the material, further proving the presence of Pd(0) on the surface. Nevertheless, the presence of imidazolium moieties within the hybrid material plays a crucial role in stabilizing Pd(0) nanoparticles through electrostatic and steric interactions thus mitigating the effect of leaching.<sup>[12]</sup>

The reaction could also be performed with a catalyst loading of 0.8 mol% at 80 °C for 15 h or with 0.4 mol% catalyst at 100 °C for 15 h. In these cases, however, catalyst deactivation already occurred after the third or second recycle, respectively (Scheme 5). Accordingly, with 0.8% catalyst, after the fourth recycle, palladium was completely reduced to unreactive Pd(0) as confirmed by XPS analysis (Figure 5a). The TEM image (Figure 5b) shows a black material due to the presence of Pd(0) nanoparticles.

The conditions reported in Scheme 4 were then extended to other differently substituted  $\beta$ -amino alcohols **1b–o**. The results obtained, shown in Table 1, confirmed the generality of our method, with the corresponding 2-oxazolidinones **2b–o** being obtained in yields ranging from 65% to 91%. In some cases, catalyst recyclability was also successfully verified. The reaction also worked nicely for the conversion of 2-aminopyridin-3-ol (**1p**) to oxazolo[4,5-*b*]pyridin-2(3*H*)-one (**2p**) (Table 1, entry 16).

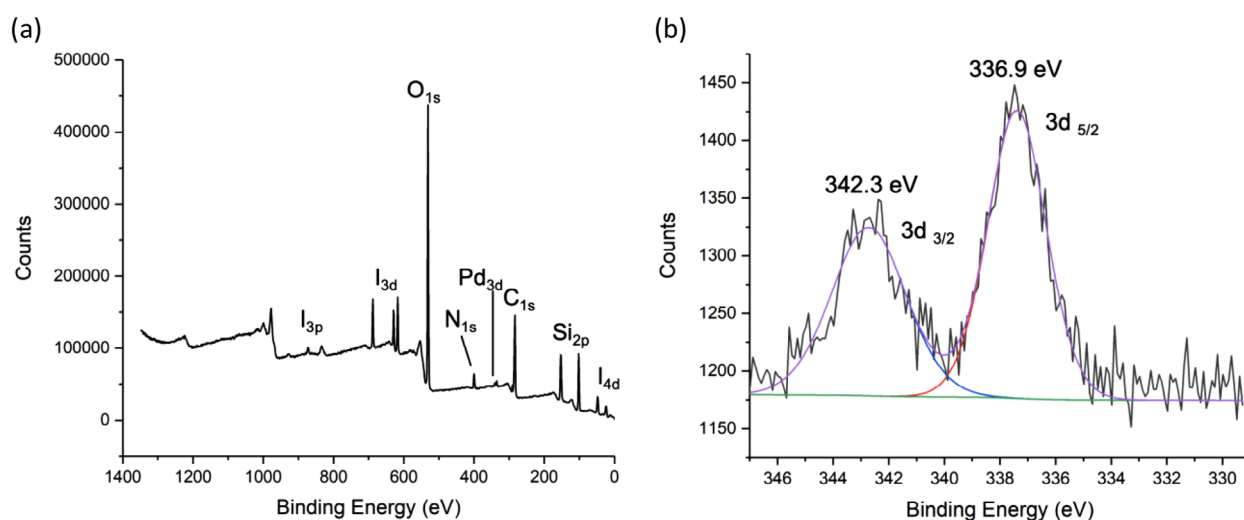


Figure 2. (a) XPS survey spectra and (b) high-resolution XPS of the Pd<sub>3d</sub> region of Pd@SiO<sub>2</sub>-POSS-imi-I (6).

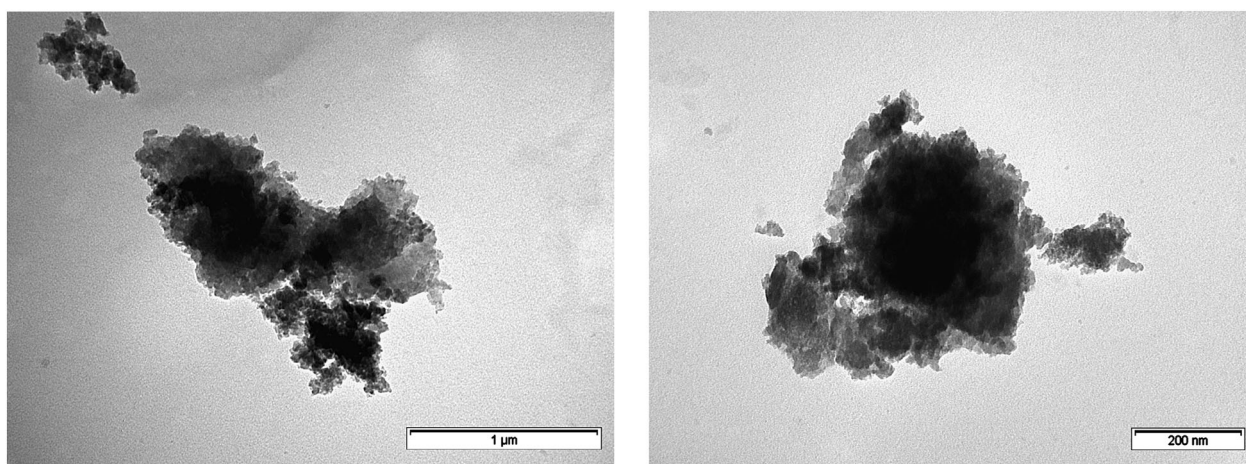
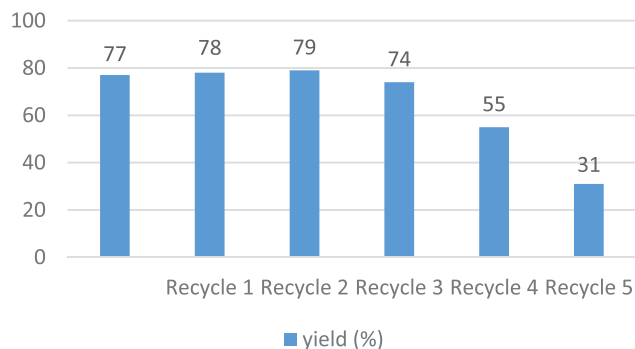
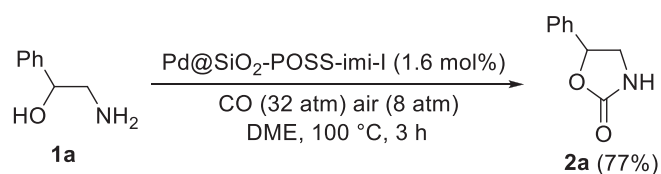


Figure 3. TEM images of Pd@SiO<sub>2</sub>-POSS-imi-I (6).

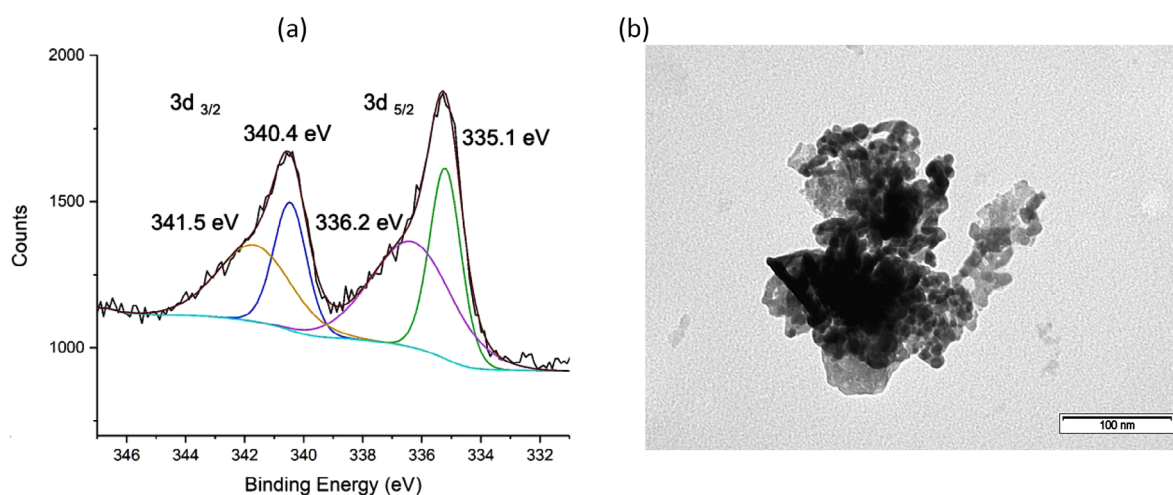


Scheme 4. Pd@SiO<sub>2</sub>-POSS-imi-I catalyzed oxidative carbonylation of 2-amino-1-phenylethan-1-ol (1a) to 5-phenyloxazolidin-2-one (2a).

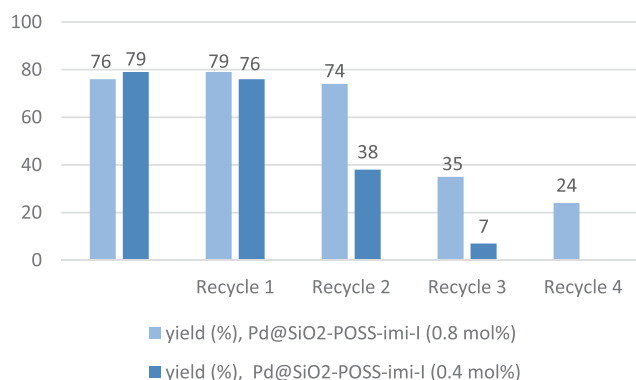
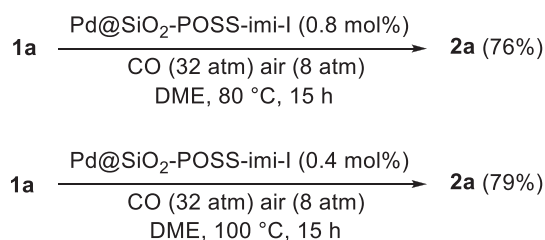
We finally analyzed the amount of residual palladium present in some representative products, 2a, 2h, and 2j in particular, by ICP-OES. In all cases, palladium contamination was very low (<1 ppm), making the oxazolidinones synthesized with our method directly suitable for possible applications in the pharmaceutical field, where a degree of palladium contamination <10 ppm is required.<sup>[13]</sup>

### 3. Conclusions

In conclusion, we have developed a PdI<sub>4</sub><sup>2-</sup>-based heterogeneous catalyst, Pd@SiO<sub>2</sub>-POSS-imi-I 6, obtained by the reaction between hybrid material SiO<sub>2</sub>-POSS-imi-I 5 with K<sub>2</sub>PdI<sub>4</sub>. This new heterogeneous catalyst 6 has proved active for the conversion of β-amino alcohols 1 into high value added 2-oxazolidinones 2, with the possibility to be recycled several times. The method has been successfully applied to a variety of β-amino alcohols as well as to 2-aminopyridin-3-ol. No appreciable palladium contamination (<1 ppm) was observed in the synthesized oxazolidinones,



**Figure 4.** (a) High-resolution XPS of the Pd3d region and (b) TEM image of Pd@SiO<sub>2</sub>-POSS-imi-I (**6**) after five recycles (reaction conditions are shown in Scheme 4).



**Scheme 5.** Pd@SiO<sub>2</sub>-POSS-imi-I catalyzed oxidative carbonylation of 2-amino-1-phenylethan-1-ol (**1a**) to 5-phenyloxazolidin-2-one (**2a**) under different conditions.

as confirmed by ICP-OES analysis of representative products, making our method useful for pharmacological applications.

Under the optimized conditions, catalyst deactivation began to occur after the fourth recycle, owing to palladium reduction to unreactive Pd(0) species, as evidenced by analysis of the recycled catalyst by XPS. These evidences indicate that in situ reduction to Pd(0) plays a key role while initially starting from Pd(II), and it is likely that reoxidation of Pd(0) limits the process and an efficient recycling. Eventually, the formation of stabilized Pd NPs tends to limit the use of this system continuously, because the presence of imidazolium groups works against the catalyst reuse, despite their stabilizing effect towards leaching. Further studies

will be needed in the future in order to develop a more robust catalytic material, less prone to undergo palladium deactivation and therefore allowing a more efficient catalyst recycling.

## 4. Experimental Section

### 4.1. Preparation of Pd<sub>4</sub>@SiO<sub>2</sub>-POSS-imi-I Catalyst (**6**)

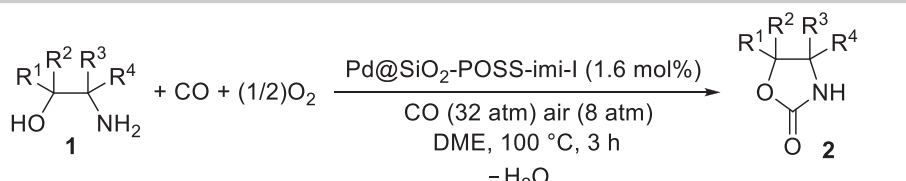
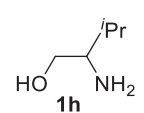
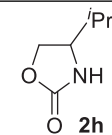
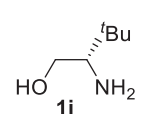
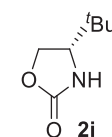
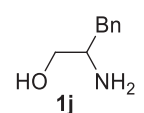
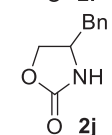
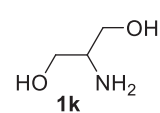
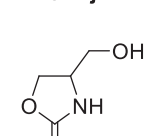
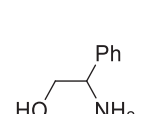
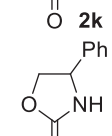
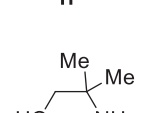
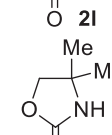
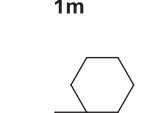
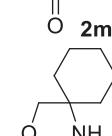
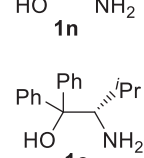
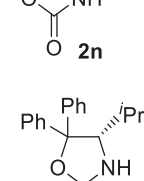
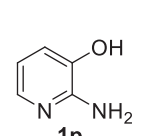
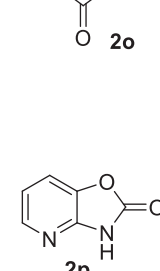
In a round-bottom flask, a suspension of supported imidazolium-modified SiO<sub>2</sub>-POSS-imi-I **5**<sup>[10a]</sup> (1 g) in MeCN (38 mL) was sonicated for 10 min. Then, K<sub>2</sub>PdI<sub>4</sub> (250 mg, 0.361 mmol) was added to the suspension. The reaction mixture was heated at 60 °C in dark under stirring for 4 days. The solid was recovered by centrifugation and washed with hot MeCN, hot MeOH, H<sub>2</sub>O, MeOH, MeCN and Et<sub>2</sub>O. Before each centrifugation, the suspension of the solid was shortly sonicated. The obtained PdI<sub>4</sub>@SiO<sub>2</sub>-POSS-imi-I **6** was dried at 60 °C under vacuum. The final material was crushed in an agate mortar and obtained as a gray solid.

### 4.2. Carbonylation Procedure

#### 4.2.1. General Procedure for the PdI<sub>4</sub>@SiO<sub>2</sub>-POSS-imi-I Catalyzed Oxidative Carbonylation of $\beta$ -amino Alcohols **1a-p**

A 35 mL stainless-steel autoclave was charged in the presence of air with PdI<sub>4</sub>@SiO<sub>2</sub>-POSS-imi-I **6** (66.0 mg, 2.59 wt% Pd,  $1.6 \times 10^{-2}$  mmol Pd) and a solution of the amino alcohol **1** (1.0 mmol; **1a**, 137.2 mg; **1b**, 61.2 mg; **1c**, 75.1 mg; **1d**, 89.1 mg; **1e**, 75.0 mg; **1f**, 89.0 mg; **1g**, 103.2 mg; **1h**, 103.0 mg; **1i**, 117.2 mg; **1j**, 151.2 mg; **1k**, 91.1 mg; **1l**, 137.2 mg; **1m**, 89.1 mg; **1n**, 129.2 mg; **1o**, 254.5 mg; **1p**, 110.1 mg) in DME (3.3 mL). The autoclave was sealed and, while the mixture was stirred, was pressurized with CO (32 atm) and air (up to 40 atm). After being stirred at 100 °C for 3 h, the autoclave was cooled, degassed, and opened. The reaction mixture was taken up with AcOEt until a total volume of ca. 15 mL, and the catalyst was separated from the reaction mixture by centrifugation at 8000 rpm for 15 min. The catalyst was taken up with AcOEt (5 mL), sonicated, separated, and washed again with AcOEt (5 mL). After sonication and separation, the catalyst was dried under a high vacuum for 2 h before being resubmitted to the reac-



Table 1. (Continued)			
			
Entry	1	2	Yield of 2 (%) <sup>a)</sup>
8			69 (67, 68, 65)
9			90
10			82 (78, 77, 75)
11			65
12			78 (76, 75, 73)
13			78
14			80
15			73
16			75 (76, 75, 71)

All reactions were carried out in DME (0.30 mmol of 1 at the start per mL of solvent) at 100 °C for 3 h, under 40 atm of a 4:1 mixture of CO-air and in the presence of 1.6 mol% of Pd@SiO<sub>2</sub>-POSS-imi-I.

<sup>a)</sup> Isolated yields based on starting 1. Values given in parentheses are the yields obtained in the recycling experiments (see text for details).

tion conditions for the recycling experiments. All the supernatant solutions were collected, the solvent was evaporated, and the products **2a–p** were purified by column chromatography on silica gel using as eluent hexane–AcOEt from 60:40 to 40:60 (for **2a–j**, **2m**, and **2n**), CH<sub>2</sub>Cl<sub>2</sub>–acetone from 70:30 to 50:50 (for **2k**), hexane–AcOEt from 70:30 to 50:50 (for **2l**), hexane–AcOEt from 100:0 to 90:10 (for **2o**), hexane–AcOEt from 20:80 to 0:100 (for **2p**).

The characterization data for new products **2g** and **2o** are given here, whereas the characterization data for known oxazolidinones are given in the [Supporting Information](#).

**(S)-4-Propyloxazolidin-2-one (2g):** Yield 121.0 mg, starting from 103.2 mg of (S)-2-aminopentan-1-ol (**1g**) (94%, Table 1 entry 7). Yellow oil. IR (film):  $\nu = 3279$  (m, br), 1751 (vs), 1483 (w), 1408 (m), 1249 (m), 1145 (w), 1016 (m), 941 (m), 773 (w) cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm): 6.90 (s, br, 1H), 4.48 (t,  $J = 8.3$ , 1H), 4.06–3.97 (m, 1H), 3.93–3.83 (m, 1H), 1.65–1.48 (m, 2H), 1.47–1.27 (m, 2H), 0.95 (t,  $J = 7.2$ , 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm): 160.6, 70.4, 52.6, 37.5, 18.6, 13.8; GC-MS:  $m/z = 129$  (M<sup>+</sup>, 23), 87 (99), 86 (100), 85 (62), 70 (17), 58 (95); HRMS-ESI ( $m/z$ ): [(M + H)<sup>+</sup>] calcd for (C<sub>6</sub>H<sub>12</sub>NO<sub>2</sub>)<sup>+</sup>: 130.0863; found, 130.0863.  $[\alpha]_D^{20}$  (acetone,  $c = 7.20 \times 10^{-3}$  g•mL<sup>-1</sup>) = -125°cm<sup>2</sup> g<sup>-1</sup>.

**(S)-4-Isopropyl-5,5-diphenyloxazolidin-2-one (2o):** Yield 205.4 mg, starting from 254.5 mg of 2-amino-3-methyl-1,1-diphenylbutan-1-ol (**1o**) (73%, Table 1, entry 15). White solid, mp = 219–220 °C. IR (KBr):  $\nu = 3294$  (m, br), 1765 (s), 1745 (s), 1659 (w), 1468 (m), 1451 (w), 1365 (w), 1252 (w), 1040 (w), 1003 (m), 944 (m), 764 (m), 743 (m); <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  (ppm): 8.10 (s, br, 1H), 7.68–7.62 (m, 2H), 7.49–7.43 (m, 2H), 7.40–7.31 (m, 4H), 7.31–7.21 (m, 2H), 4.43 (s, 1H), 1.89–1.77 (m, 1H), 0.90 (d,  $J = 6.8$ , 3H), 0.50 (d,  $J = 6.4$ , 3H); <sup>13</sup>C NMR (125 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  (ppm): 157.3, 145.3, 139.7, 128.3, 128.0, 127.6, 127.1, 125.5, 125.0, 87.6, 64.1, 29.0, 20.1, 14.4; GC-MS:  $m/z = 281$  (M<sup>+</sup>, 3), 238 (2), 183 (100), 165 (26), 105 (67), 77 (24); HRMS-ESI ( $m/z$ ): [(M + H)<sup>+</sup>] calcd for (C<sub>18</sub>H<sub>20</sub>NO<sub>2</sub>)<sup>+</sup>: 282.1489; found, 282.1491.  $[\alpha]_D^{20}$  (DMSO,  $c = 7.96 \times 10^{-3}$  g•mL<sup>-1</sup>) = -163°cm<sup>2</sup> g<sup>-1</sup>.

#### 4.2.2. Pd<sub>4</sub>@SiO<sub>2</sub>-POSS-lmi-I Catalyzed Oxidative Carbonylation of 2-Amino-2-phenylethan-1-ol (1l) in Larger Scale

A 300 mL stainless steel autoclave was charged in the presence of air with Pd<sub>4</sub>@SiO<sub>2</sub>-POSS-lmi-I (**6**) (328.6 mg, 2.59 wt% Pd,  $1.6 \times 10^{-2}$  mmol Pd) and a solution of 2-amino-2-phenylethan-1-ol (**1l**) (5.0 mmol, 686 mg) in DME (16.7 mL). The autoclave was sealed and, while the mixture was stirred, was pressurized with CO (32 atm) and air (up to 40 atm). After being stirred at 100 °C for 3 h, the autoclave was cooled, degassed, and opened. The reaction mixture was taken up with AcOEt until a total volume of ca. 25 mL, and the catalyst was separated from the reaction mixture by centrifugation at 8000 rpm for 15 min. The catalyst was taken up with AcOEt (15 mL), sonicated, separated, and washed again with AcOEt (15 mL). All the supernatant solutions were collected, the solvent was evaporated, and the product was purified by column chromatography on silica gel using as eluent hexane–AcOEt from 70:30 to 50:50. 4-Phenyloxazolidin-2-one (**2l**) was recovered with an isolated yield of 83% (673 mg).

## Acknowledgements

Financial support by MUR, PRIN 20223B4JWC project (Valorization of Carbon Oxides by Sequential Catalysis: Combining the Reverse Water Gas Shift Reaction with Catalytic Carbonylation for

the Synthesis of High Value Added Compounds—COXSECAT) to B.G. is acknowledged. Thanks are due to Prof. Antonio Palumbo Piccionello (University of Palermo, Italy) for HRMS measurements.

Open access publishing facilitated by Università della Calabria, as part of the Wiley - CRUI-CARE agreement.

## Conflict of Interests

The authors declare no conflict of interest.

## Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Keywords:** Carbonylation · Heterogeneous catalysis · 2-Oxazolidinones · Oxidative carbonylation · Palladium

- [1] G. F. S. Fernandes, C. B. Scarim, S.-H. Kim, J. Wu, D. Castagnolo, *RSC Med. Chem.* **2014**, *23*, 823–847.
- [2] For recent examples, see: a) P. Prasher, M. Sharma, *Drug Dev. Res.* **2023**, *84*, 1337–1345; b) D. A. Negatu, W. W. Aragaw, J. Cangialosi, V. Dartois, T. Dick, *Antimicrob. Agents Chemother.* **2023**, *67*, e0165522; c) A. R. N. Ndukwe, S. Wiedbrauk, N. R. B. Boase, K. E. Fairfull-Smith, *Chem. Asian J.* **2022**, *17*, e202200201.
- [3] a) B. Armentano, R. Curcio, M. Brindisi, R. Mancuso, V. Rago, I. Ziccarelli, L. Frattaruolo, M. Fiorillo, V. Dolce, B. Gabriele, A. R. Cappello, *Biomedicines* **2020**, *8*, 35; b) N. A. Al-Hasawi, O. A. Phillips, F. Al-Awadhi, L. H. Sharaf, S. A. Amine, L. Novotny, *Anticancer Res.* **2020**, *40*, 5125–5140.
- [4] For reviews, see: a) A. Nazari, M. M. Heravi, V. Zadsirjan, *J. Organomet. Chem.* **2021**, *932*, 121629; b) V. Zadsirjan, M. M. Heravi, *Curr. Org. Synth.* **2018**, *15*, 3–20; c) M. M. Heravi, V. Zadsirjan, B. Farajpour, *RSC Adv.* **2016**, *6*, 30498–30551.
- [5] *Carbon Monoxide in Organic Synthesis—Carbonylation Chemistry* (Ed: B. Gabriele), Wiley-VCH, Weinheim **2022**.
- [6] For a very recent review, see: a) B. Gabriele, *Tetrahedron Chem* **2024**, *12*, 100107; b) B. Gabriele, G. Salerno, D. Brindisi, M. Costa, G. P. Chiusoli, *Org. Lett.* **2000**, *2*, 625–627; c) B. Gabriele, R. Mancuso, G. Salerno, M. Costa, *J. Org. Chem.* **2003**, *68*, 601–604; d) R. Mancuso, D. S. Raut, N. Della Ca', F. Fini, C. Carfagna, B. Gabriele, *ChemSusChem* **2015**, *8*, 2204–2211.
- [7] P. Kushwaha, *Curr. Pharm. Anal.* **2020**, *17*, 960–968.
- [8] I. Ziccarelli, R. Mancuso, F. Giacalone, C. Calabrese, V. La Parola, A. De Salvo, N. Della Ca', M. Gruttadauria, B. Gabriele, *J. Catal.* **2022**, *413*, 1098–1110.
- [9] The flammability range of CO in air mixtures is 16.3–70 vol% at room temperature and atmospheric pressure, and becomes smaller at higher pressure (e.g., it is 20–60 vol% at 20 atm). See: C. M. Bartish, G.M. Drissel, in *Kirk-Othmer Encyclopedia of Chemical Technology*, 3rd ed., (Eds: M. Grayson, D. Eckroth, G.J. Bushey, L. Campbell, A. Klingsberg, L. van Nes), Vol. 4, Wiley, New York **1978**, pp. 774–775.
- [10] a) C. Calabrese, L. F. Liotta, F. Giacalone, M. Gruttadauria, C. Aprile, *ChemCatChem* **2019**, *11*, 560–567; b) C. Calabrese, V. Campisciano, F. Siragusa, L. F. Liotta, C. Aprile, M. Gruttadauria, F. Giacalone, *Adv. Synth. Catal.* **2019**, *361*, 3758–3767.
- [11] a) V. Campisciano, C. Calabrese, L. F. Liotta, V. La Parola, M. Gruttadauria, F. Giacalone, *App. Organomet. Chem.* **2019**, *33*, e4848; b) F. Giacalone, V. Campisciano, C. Calabrese, V. La Parola, L. F. Liotta, C. Aprile, M. Gruttadauria, *J. Mater. Chem. A.* **2016**, *4*, 17193–17206; c) M. Xu, J. Zhao, G. Shu, X. Zheng, Q. Liu, Y. Wang, M. Zeng, *Int. J. Biol. Macromol.* **2019**, *125*, 213–220; d) V. Campisciano, R. Burger, C. Calabrese, L. F. Liotta, P.

- Lo Meo, M. Gruttaduria, F. Giacalone, *Nanoscale Adv* **2020**, *2*, 4199–4211; e) A. Morena, V. Campisciano, A. Comès, F. Liotta, M. Gruttaduria, C. Aprile, F. Giacalone, *Nanomaterials* **2021**, *11*, 2243.
- [12] a) S. Özkur, R. G. Finke, *J. Am. Chem. Soc.* **2002**, *124*, 5796–5810; b) M.-A. Neouze, *J. Mater. Chem.* **2010**, *20*, 9593–9607; c) C. J. Serpell, J. Cookson, A. L. Thompson, C. M. Brown, P. D. Beer, *Dalton Trans.* **2013**, *42*, 1385–1393; d) L. S. Ott, R. G. Finke, *Coord. Chem. Rev.* **2007**, *251*, 1075–1100; e) F. Giacalone, M. Gruttaduria, *ChemCatChem* **2016**, *8*, 664–684.
- [13] A limit of 10 ppm is recommended by the US Pharmacopeia (<https://www.usp.org/sites/default/files/usp/document/our-work/chemical-medicines/key-issues/c232-usp-39.pdf>) as well as the Euro-

pean Medicines Agency ([https://www.ema.europa.eu/en/documents/scientific-guideline/international-conference-harmonisation-technical-requirements-registration-pharmaceuticals-human-use-ich-q3d-elemental-impurities-step-5-revision-1\\_en.pdf](https://www.ema.europa.eu/en/documents/scientific-guideline/international-conference-harmonisation-technical-requirements-registration-pharmaceuticals-human-use-ich-q3d-elemental-impurities-step-5-revision-1_en.pdf)) for oral drug products and for a maximum daily dose of not more than 10 g/day.

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Manuscript received: November 05, 2024

Revised manuscript received: December 18, 2024

Accepted manuscript online: December 19, 2024

Version of record online: December 30, 2024