

# POLITAG-Pd(0) catalyzed continuous flow hydrogenation of lignin-derived phenolic compounds using sodium formate as a safe H-source

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## ABSTRACT

Phenols are aromatic biobased compounds and as they are accessible from lignin depolymerization, they can be a useful platform chemicals to produce value-added products. Herein we report our recent investigations on the definition of an approach to the efficient continuous flow selective hydrogenation of phenols in water. Our protocol is based on the use of sodium formate as a clean and safe hydrogen source in combination with our newly defined heterogeneous POLITAG-Pd(0) catalytic system. POLITAG is a polymeric heterogeneous support decorated with pincer-type ionic ligands proven to be highly efficient for the stabilization of Pd(0) nanoparticles. The results obtained are remarkable in comparison with other protocols that employ sodium formate as H-source. Indeed, our investigation has been extended to a variety of differently substituted phenolic compounds that have been hydrogenated with excellent to good selectivity in continuous flow conditions. Durability of the catalyst has been also tested with a representative continuous processing of over 100 mmol that showed no loss in efficiency and minimal metal leaching.

## 1. Introduction

The replacement of petrol-based chemicals and fuel with renewable sources is the challenge of the modern chemistry. Biomass is a renewable feedstock that can be used both for energy [1–4] and production of fundamental bulk and commodity chemicals [3,4]. In the context of a sustainable production, lignocellulosic biomass represents an ideal carbon-neutral alternative to reduce the environmental impact associated to the chemical industry.

Among biomass-derived feedstock, phenols are aromatic compounds which can be easily upgraded to obtain different value-added chemicals [4]. Generally, bioderived phenols are considered as waste from lignin treatment to access cellulose or related sugar polymers and, therefore their usage as possible platform chemicals for further transformation to target materials, is nowadays highly desirable [5–11]. Indeed, most of the processes involving lignin valorization, aim to the production of bioderived-oil with high H/C ratio in order to both improve the thermal stability and reduce the viscosity to eventually increase miscibility with petrol-based fuels [5–11].

Aqueous formic acid and its salt derivatives are interesting hydrogen-sources that, also derived from biomasses, can be considered as

promising and safe alternative to classical molecular hydrogen [12–27]. Formic acid and formates feature a good stability and the latter, also low toxicity [28]. They are included among the liquid organic hydrogen sources (LOHC), ideal alternatives for a safe handling and transport of hydrogen equivalents [29–31]. Within the context of a sustainable approach, aqueous formic acid obtained from biomass is of major interest [28]. When in combination with an appropriate catalytic system, formic acid derivatives may offer an effective technology to produce molecular hydrogen under controlled conditions and at the same time utilize this H-source for a concomitant hydrogenation where the catalytic system may control the process efficiency and selectivity.

Among the processes involving phenols valorization, the selective hydrogenation to cyclohexanone [22–27] is of great interest. Indeed, cyclohexanone is a key product in the preparation of largely interesting Nylon 6, Nylon 6,6 and polyamide resins [32]. Selective hydrogenation of phenols to the corresponding cyclohexanones, constitutes an advantage in terms of step-economy, waste disposal costs and purification procedures, if compared to a classic two step processes comprising the over-reduction to cyclohexanol and subsequent dehydrogenation to cyclohexanone [33].

On the other hand a step-economical and effective strategy can be

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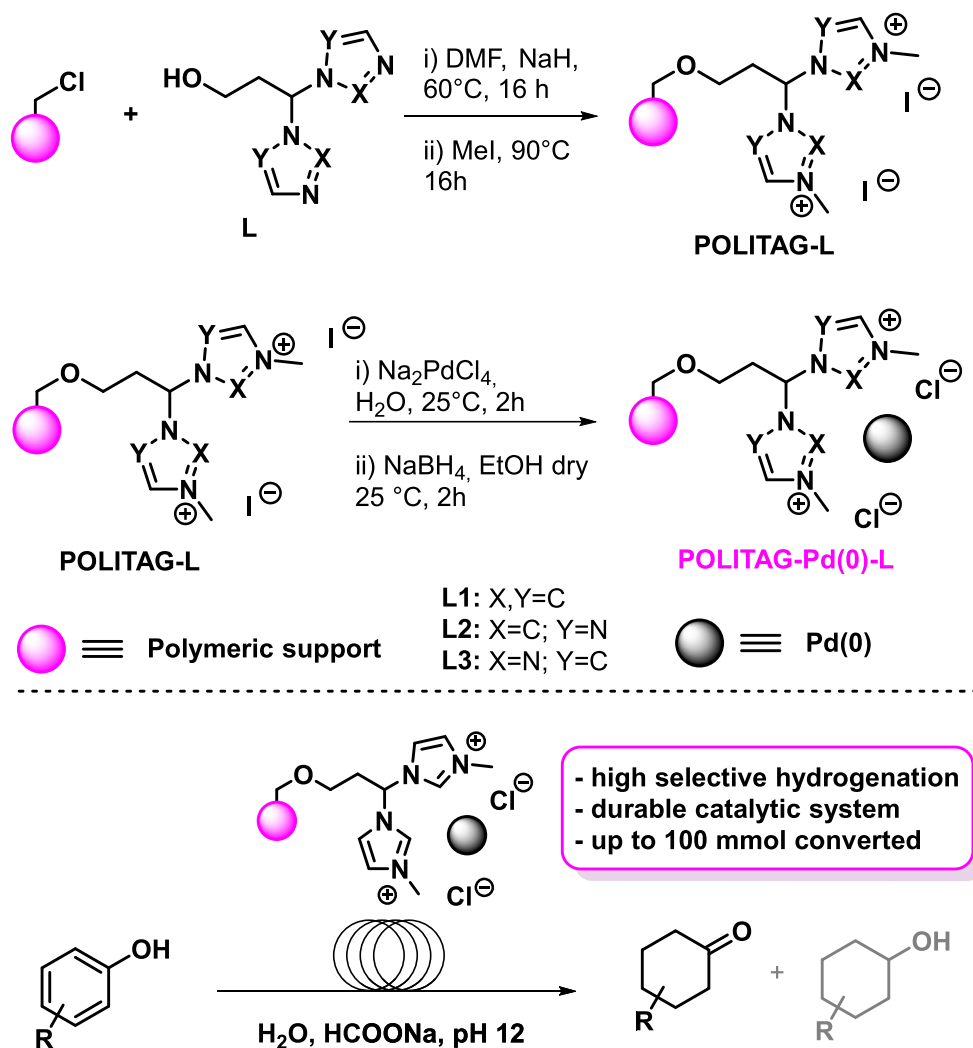


Fig. 1. Schematic representation of POLITAGs-Pd(0) synthesis and features of the current work.

defined using direct selective hydrogenation based on use of an heterogeneous catalytic system. This process may become very efficient if the absorption of phenolate ion onto the catalyst and its effective reduction can be combined with the prompt desorption of the initially formed cyclohexanone before further hydrogenation process may lead to the cyclohexanol formation [34]. This absorption/desorption equilibrium strongly depends on the nature of the heterogeneous catalyst support and therefore at this aim, different catalytic systems have been developed and/or tested for the use with formic acid or formates [22–27].

Generally, besides the reduction of simple phenol, when the conditions are extended to variously substituted oxygenated phenolic compounds, it is more difficult to obtain high levels of selectivity depending on the nature and position of the substituent and also to the additional need for longer reaction times.

Our research is mainly dedicated to the development of sustainable protocols by exploiting flow technology [35] to enable and easily control the reaction parameters that could steer to highly efficient and selective processes. Accordingly, we have been investigating the definition of effective catalytic systems and their use in flow reactors to access the selective hydrogenation of phenols. In fact, flow reactors may guarantee the accurate control of the reaction conditions with an ideal interaction between reagents and catalyst especially when they are in different phases [35–39]. In fact, this is one of the crucial aspects in the hydrogenation reaction using heterogeneous catalysts, where substrates are in

solution and gaseous hydrogen is generated at the heterogeneous support while at equilibrium with liquid and gas phases. In flow conditions, hydrogen developed during the reaction is confined into the reactor where appropriate temperature and pressure can be precisely controlled. To the best of our knowledge, also in the cases where flow reactors are employed in the hydrogenation of phenols with formates as H-source, the extension of the reaction conditions to different phenolic compounds is difficult [26] leading to unsatisfactory conversion and/or selectivity for most of the substituted phenol derivatives.

Herein we report the preparation of a POLITAG-Pd(0) heterogeneous catalytic system and its use in the selective hydrogenation of different phenolic compounds under flow conditions using water as a safer reaction medium and sodium formate as a safe H-source (Fig. 1). POLITAGs [40–42] are polymer-based heterogeneous catalysts featuring a pincer type ionic ligands that we have developed and proved to be effective for the stabilization of both Pd(II) anionic complex [41,42] and Pd(0) nanoparticles [40]. We have reported that these catalysts show good performance in catalyzing cross-coupling [40,41] and C–H activation [42] reactions. Due to the ligands architecture and the stability showed, we decided to investigate the use of these systems in the selective transfer hydrogenation of phenols under flow condition using sodium formate as H-source.

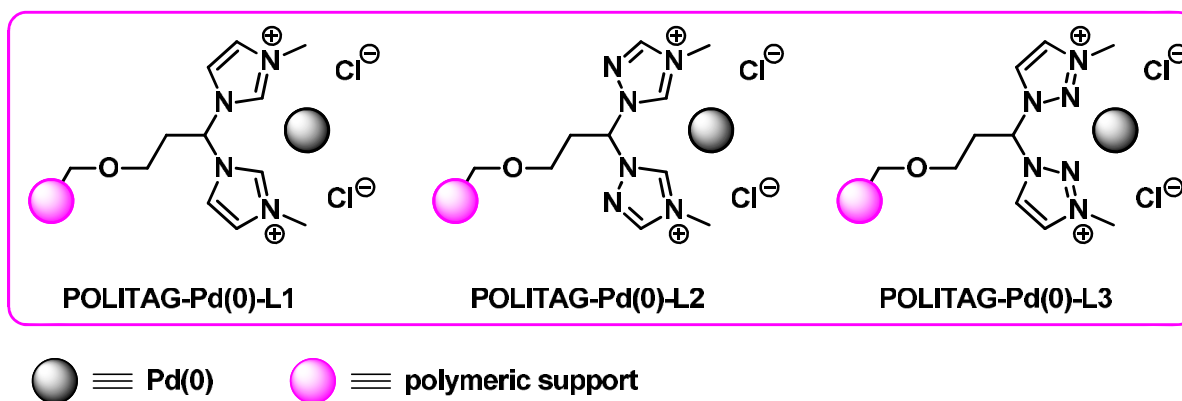


Fig. 2. POLITAGs-Pd(0) architectures.

## 2. Experimental section

### 2.1. General remarks

All chemicals were used without any further purification unless otherwise noted. 4-Vinylbenzylchloride (VBC) and styrene (STY) were extracted three times with a 10% w/w NaOH solution and filtered through Al<sub>2</sub>O<sub>3</sub> pad to remove the polymerization inhibitor (tert-butyl catechol). Dibenzoylperoxide was re-crystallized from methanol. GC analyses were performed using a Hewlett-Packard HP 5890A equipped with a capillary column DB 35MS (30 m, 0.32 mm), a FID detector and helium as a gas carrier. GC-EIMS analyses were carried out using a Hewlett-Packard HP 6890 N Network GC system/5975 Mass Selective Detector equipped with an electron impact ionizer at 70 eV. Elemental Analysis (EA) were conducted on Elementar UNICUBE® elemental analyzer. Palladium content was measured by using an Agilent 4210 MP-AES instrument. TEM images were obtained using a PHILIPS CM 12 transmission electron microscopy operating in the range 20 to 120 kV with an image resolution of 0.34 nm.

### 2.2. General procedure for the hydrogenation in batch

Phenol (**1a**; 0.4 mmol, 37.65 mg), sodium formate (**2**, 68 mg, 2.5 equiv.), and water (0.2 M, 2 mL) were placed in a 2 mL screw-capped vial equipped with a magnetic stirrer. The mixture was adjusted to pH 12.0 by adding 5 M aq NaOH. POLITAG-Pd(0)-L1 (5 mol%) was added, and the mixture was kept under stirring at 120 °C. After for 4 h the mixture was cooled, and the catalyst was filtered off. The product was recovered by extraction with heptane and evaporation of the solvent under reduced pressure.

### 2.3. General procedure for the POLITAG Pd(0)-L1 recycle study

Phenol (**1a**, 0.4 mmol, 37.65 mg), sodium formate (**2**; 68 mg, 2.5 equiv.), and water (0.2 M, 2 mL) were placed in a 2 mL screw-capped vial equipped with a magnetic stirrer. The mixture was adjusted to pH 12.0 by adding 5 M aq NaOH. POLITAG-Pd(0)-L1 (5 mol%) was added, and the mixture was kept under stirring at 120 °C. After for 4 h the mixture was cooled, and centrifuged (15 min, 6500 rpm). After the supernatant removal, the catalyst was washed with 1 mL of water, dried under vacuum at 80 °C for 3 h and reused in the next run.

### 2.4. General procedure for the flow hydrogenation

A premixed mixture of phenolic compound (**1a-h**) and sodium formate (**2**, 3 equiv.) in H<sub>2</sub>O (0.1 M) was prepared in a flask with the function of the reservoir, and the mixture was adjusted to pH 12.0 with the addition of 5 M aq NaOH. POLITAG-Pd(0)-L1 (8 wt%, 0.54 mmol, 718.3 mg) was dispersed in solid glass beads and glass powder and was charged in a stainless-steel reactor; the equipment was connected by using the appropriate valves, and a backpressure regulator was placed on the outlet tube. The packed reactor was placed into a thermostated box, and the mixture was pumped through the catalyst columns at 120 °C. The conversion of **1a-i** and its selectivity were periodically monitored by GLC analysis.

## 3. Results and discussion

A preliminary optimization study was conducted in batch conditions where we investigated the catalytic efficiency of different POLITAG-Pd(0) systems using three different heterocyclic pincer ligands (Fig. 2). We

**Table 1**

Screening of POLITAGs-Pd(0) catalysts for the selective hydrogenation of phenol (**1a**) with sodium formate (**2**).

Entry	pH	Catalyst	T (°C)	t (h)	Conv. (%) <sup>a</sup>	3a (%) <sup>a</sup>
1 <sup>b</sup>	12	Pd/C	90	0.5	95	98
2	12	POLITAG-Pd(0)-L1	90	4	32	100
3	12	POLITAG-Pd(0)-L1	90	18	55	100
4	12	POLITAG-Pd(0)-L1	120	4	100	100
5	12	POLITAG-Pd(0)-L2	120	4	55	50
6	12	POLITAG-Pd(0)-L3	120	4	30	100

Reaction conditions: **1a** (0.4 mmol), **2a** (2.5 eq), catalyst (5 mol%), H<sub>2</sub>O (0.2 M). <sup>a</sup>Conversion of **1a** to products was determined by GLC

<sup>b</sup> ref. [23].

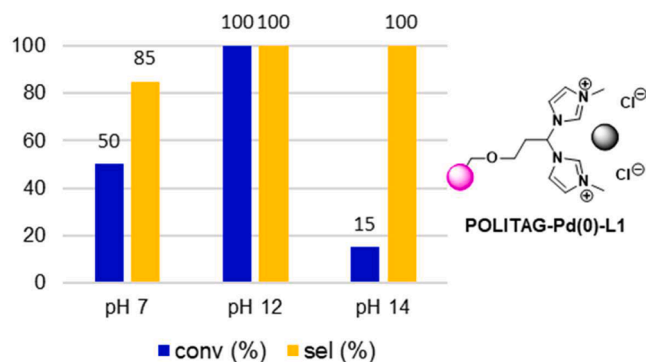


Fig. 3. pH screening using NaOH as base.

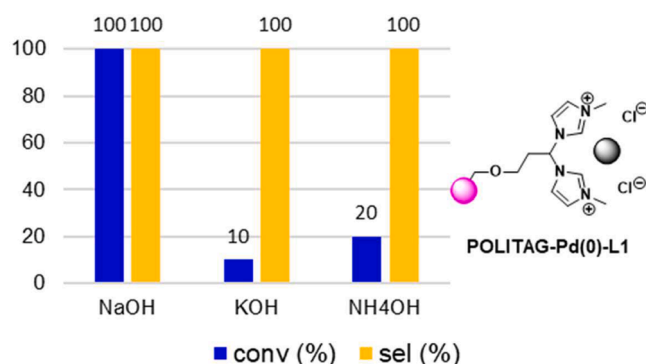


Fig. 4. Screening of base at pH 12.

compared these systems searching for the most promising reaction conditions suitable for being transferred into a continuous-flow reactor system.

The catalytic activity of the three different POLITAGs-Pd(0) (Fig. 2) for the selective hydrogenation of phenol (**1a**) using sodium formate (**2**) in water as reaction medium, was tested and compared also to the results obtained in our previous work (Table 1) [26].

While POLITAG-Pd(0)-L1, featuring a bis-imidazolium ionic tag ligand, showed at 90 °C a conversion lower to that achieved with Pd/C (Table 1, entries 2, 3 vs entry 1), it should be also noticed that a higher selectivity was achieved, suggesting a more controlled hydrogen transfer on Pd(0) nanoparticles. Indeed, by increasing the temperature to 120 °C complete conversion of phenol **1a** and good selectivity toward the desired product **3a** could be obtained (Table 1, entry 4), making this catalyst and condition more interesting.

The catalytic tests with POLITAGs-Pd(0) with L2 and L3, 1,2,4- and 1,2,3-triazolium ligands respectively, showed a reduced catalytic

efficiency both in terms of conversion (Table 1, entries 5–6) and in selectivity (Table 1, entry 5) if compared to the POLITAG-Pd(0)-L1 system based on bis-imidazolium. Given these considerations, POLITAG-Pd(0)-L1 was selected as catalytic system to further explore the phenols hydrogenation.

To have additional insights about the process, a pH screening was also conducted. Different solutions of phenol (**1a**) and sodium formate (**2**) were prepared by varying pH conditions. As illustrated in Fig. 3, pH 12 confirmed to give the best results allowing a complete conversion and selectivity toward cyclohexanone (**3a**). Increasing or reducing the pH of the solution revealed, on the contrary, a clear drop of both conversion and selectivity. When the reaction was performed at pH 7, only 50% conversion was observed with an important decrease of the selectivity to **3a**. Poor results were also obtained when pH reached the value of 14. Anyway, although the formation of the over-hydrogenated product cyclohexanol (**4a**) was not detected, the conversion did not exceed 15%.

Subsequently, the role of the base used to set the ideal pH 12 conditions was considered (Fig. 4).

Only NaOH gave good results in terms of conversion and selectivity, confirming the efficient role of sodium to assist Pd-catalyzed hydrogen transfer while larger counter ions hamper this process [26,27]. This cation effect is in accordance with the results obtained by the pH screening (Fig. 3). Indeed, considering both the influence of pH and bases, it is strongly suggested that the reaction mechanism proceed through the absorption of phenolate ion on POLITAG support (Scheme 1). The selected pH favored the formation of the phenolate ion controlling the desorption before the formation of over-hydrogenated product, while the cation size influences its absorption close to the Pd nanoparticles driving the hydrogen-transfer process.

With the intention to test our catalytic system in the use under continuous flow conditions, we performed a preliminary catalyst recycling study. POLITAG-Pd(0)-L1 resulted active without any loss of efficiency for four representative consecutive runs (Table 2). After each cycle, the crude reaction mixture was centrifuged and subsequently the supernatant removed while the catalyst washed with water, dried under vacuum at 80 °C for 3 h and then reused in the consecutive run.

These results confirm the efficiency of the catalyst in batch but also let to presume its long-term efficiency which is essential for an effective continuous flow protocol.

The continuous flow protocol was set by packing a stainless-steel reactor with POLITAG-Pd(0)-L1 (8% wt, 0.54 mmol, 719 mg) dispersed over glass powder and beads. An aqueous solution of phenol (**1a**) and sodium formate (**2**) adjusted to pH 12.0 was placed in a flask acting as a reservoir. This was connected to a pump and the aqueous mixture let to flow through the reactor (in a thermostated chamber at 120 °C) at a rate of 0.29 mLmin<sup>-1</sup> (Fig. 5).

Given that during the reaction the formation of H<sub>2</sub> occurs, a back-pressure regulator (BPR) was placed at the end of the catalyst column, setting the pressure to 5 psi (1.0 psi = 6.9 kPa). Under these conditions

Table 2

Recovery and reuse of the catalyst for the representative selective hydrogenation of phenol (**1a**) with sodium formate (**2**).

Run	Conv (%) <sup>a</sup>	3a (%)
1	100	>99
2	100	>99
3	100	>99
4	100	>99

Reaction conditions: **1a** (0.4 mmol), **2a** (2.5 eq), catalyst (5 mol%), H<sub>2</sub>O (0.2 M).

<sup>a</sup> Conversion to products determined by GLC.

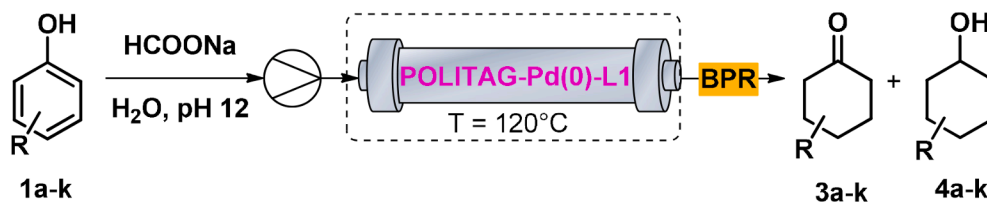


Fig. 5. Flow system used for the hydrogenation of phenols.

Table 3

Optimization for the continuous flow hydrogenation of phenol (1a).

Entry	Concentration (M)	BPR	Residence time (min)	Flow rate (mL/min)	Conv. (%)	3a (%)
1	0.2	5	40	0.29	65	100
2	0.2	20	64	0.18	100	92
3	0.2	5	64	0.18	100	100
4	0.1	5	30	0.38	85	100
5	0.1	5	45	0.26	100	100 (87) <sup>a</sup>
6	0.1	5	60	0.19	100	100
7	0.1	20	75	0.15	100	90

<sup>a</sup> Isolated yield is giving in parentheses.

only 65% conversion of phenol (1a) was observed with good selectivity toward the desired product 3a (Table 3, entry 1). In order to obtain a better conversion, the flow rate was decreased to 0.18 mLmin<sup>-1</sup> and the BPR was increased to 20 psi, in such configuration a longer residence time could be achieved. With this setup it has been possible to obtain full conversion with a slight decrease in selectivity (Table 3, entry 2). Satisfying optimal results in both conversion and selectivity, were obtained using a 5 psi BPR (entry 3). Unfortunately, after fluxing these mixtures consecutively we noticed that some clogging of the system may occur, due to the formation of sodium bicarbonate, but after washing the reactor with water efficiency could be regenerated completely. To avoid this problem, we decreased the solution concentration from 0.2 to 0.1 M and in these conditions, with a residence time of 45 min, both a complete conversion and selectivity to the product 3a were obtained. After converting representative 10 mmol of 1a pure cyclohexanone product (3a) could be isolated in an 87% yield (Table 3, entry 5). No loss in selectivity was detected also using a higher residence time of 60 min (Table 3, entry 6), while with lower flow rate and higher BPR (residence time 75 min, Table 3, entry 7) the formation of 10% of cyclohexan-1-ol (4a) occurred. These data confirm that POLITAG-Pd(0)-L1 is stable and selective even using longer residence times, conditions that can be helpful for the extension of the substrate scope.

The efficiency and stability of the supported catalyst was also confirmed by the MP-AES analysis conducted on the downstream reaction mixtures to measure Pd leached in solution. The results gave a very low (0.01 ppm) amount of Pd content and confirmed the stability of the catalytic system under the optimized conditions for phenols hydrogenation, resulting in an expected capability to operate the flow conditions for long time.

Considering the results obtained with phenol (1a), the scope of the flow protocol was extended to other phenol derivatives (see Table S1 and Scheme 2). Initially, we paid more attention to biomass derived substrates like cresols (1b-c), catechols (1d-e) and guiacols (1f-g) being directly obtained from lignin depolymerization. By using different settings obtained varying the residence time, flow rate and the BPR, we attempted the optimization of the process to reach best conversions and selectivity to the corresponding products (3). Excellent results were obtained with para (1b) and ortho-cresol (1c) by using a 5 psi BPR and applying a flow rate of 0.26 (p-cresol) and 0.32 mL min<sup>-1</sup> (o-cresol) achieving in both cases a 100% conversion and a 100% and 91% selectivity toward product 3b and 3c, respectively (Table S1, entries 2,3). These outcomes are of high interest considering that both using gaseous H<sub>2</sub> and formic acid as hydrogen source, relevant amounts of the over hydrogenation products 4b-c were detected in other literature

Table 4

Continuous flow hydrogenation of eugenol (1k).

Entry	1k BPR (psi)	Residence time (min)	Flow rate (mL/min)	Conv (%)	4k:5k (%)
1	20	40	0.29	100	100:0
2	40	95	0.12	100	80:20

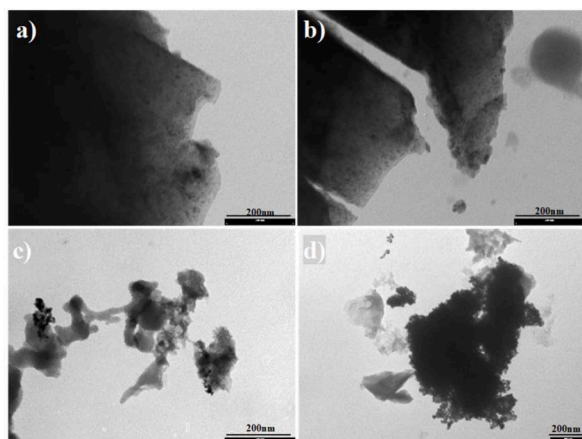


Fig. 6. TEM images of POLITAG-Pd(0)-L1 a), b) fresh and c), d) used.

reports [43,44].

In the case of catechols, 82% conversion and 80% selectivity to the product **3d**, was achieved with *p*-catechol (**1d**) by employing a 40 psi BPR and a flow rate of 0.29 mLmin<sup>-1</sup> (Table 4, entry 4). While for the regioisomer *o*-catechol (**1e**), a reduced flow rate of 0.18 mLmin<sup>-1</sup> was needed to reach a satisfactory conversion leaving the reactants in contact with the catalyst for a longer time. In this case, 84% conversion could be achieved but only 50% of the desired *o*-hydroxycyclohexan-1-one (**3e**) was accessed (Table S1, entry 5).

Among lignin derived phenols, we also tested challenging substrate guaiacols (**1f-g**). Using *p*-guaiacol (**1f**) as starting material it was possible to obtain *p*-methoxycyclohexan-1-one (**3f**) with a great selectivity of 93% and a conversion of 99% at a flow rate of 0.18 mLmin<sup>-1</sup> (Table S1, entry 7). If the flow rate was increased sufficient conversion into the product was not satisfactory (Table S1, entry 6). The same issues were encountered with *o*-guaiacol (**1g**), and satisfactory results in terms of conversion and selectivity were achieved with a long resident time of 106 min (Table S1, entry 9).

To further investigate the applicability of our flow system also halogenated phenols were screened. In fact, these substrates may be

useful to further evaluate the chemoselectivity of the system when also a typical dehalogenation process can occur. This reaction can be also of additional interest as it allows to convert these anthropogenic pollutants into value added chemicals and manipulate waste or dangerous substance into new interesting chemicals [45–47].

At this aim, the developed flow protocol proved to be efficient for the one-pot conversion of *o*-chloro (**1h**) and *o*-bromophenol (**1i**) into cyclohexanone (**3a**) (Scheme 3). In both cases a residence time of 20 min led to a very good conversion of 80% and 75%, respectively with no formation of the undesired by-product cyclohexan-1-ol (**4a**).

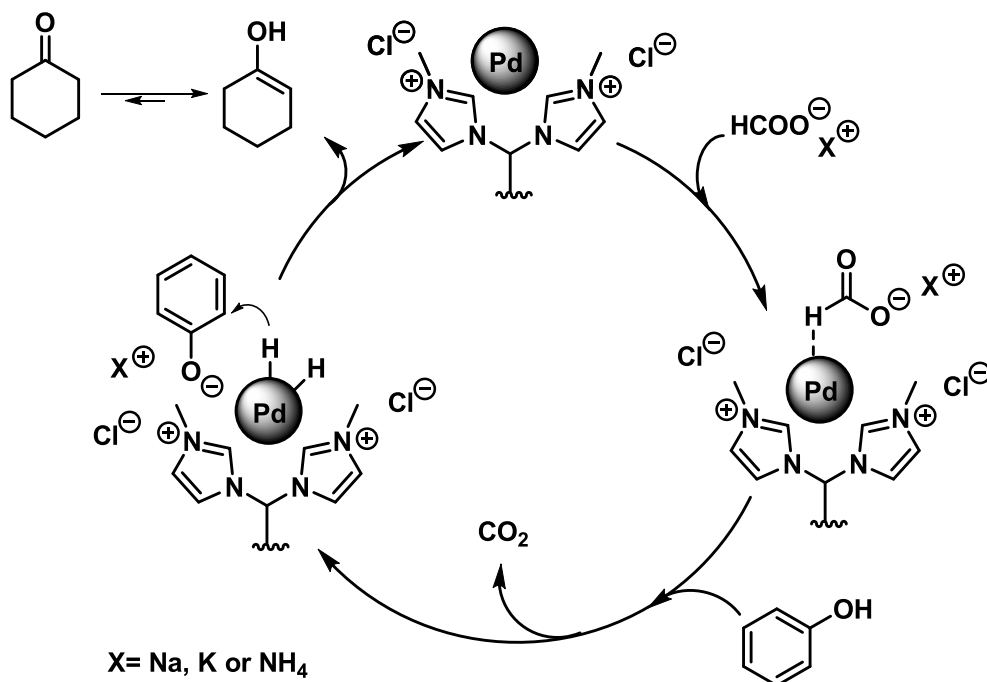
Additionally, we also looked for more information about our protocol and catalyst, by studying the hydrogenation of 1-naphtol (**1j**) and eugenol (**1k**). In the first case, it was possible to achieve a conversion of 70% exploiting a 40 psi BPR and a flow rate of 0.12 mLmin<sup>-1</sup> (Scheme 4), with a 70% formation of the desired product 3,4-dihydronaphtalen-1(2H)-one (**3j**).

Concerning eugenol (**1k**), with a BPR of 20 PSI and a flow rate of 0.29 mLmin<sup>-1</sup>, was not possible to selective hydrogenate the phenolic ring, but only the olefinic double bond obtaining the 2-methoxy-4-propylphenol (**4k**) (Table 4, entry 1).

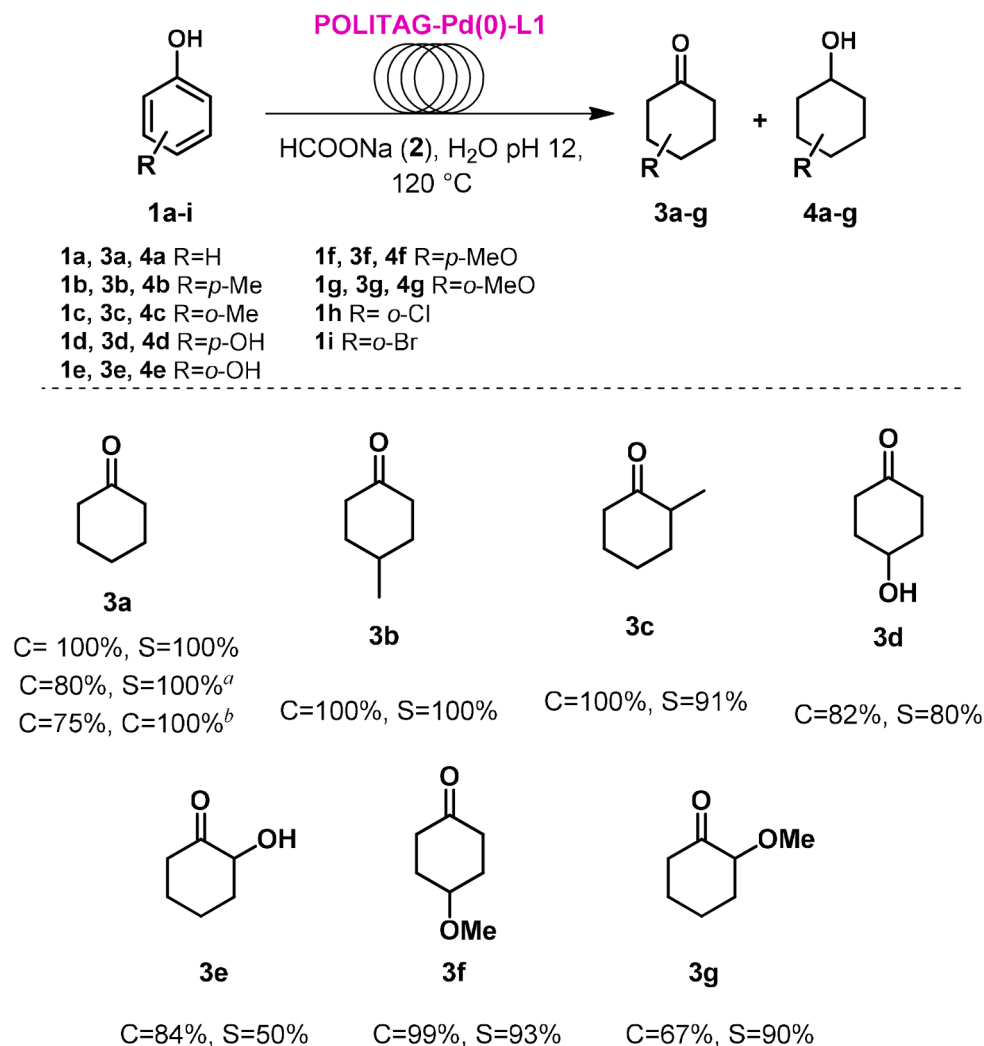
With a residence time increased from 40 to 95 min (0.12 mLmin<sup>-1</sup>), only a partial hydrogenation of the phenolic ring was achieved as well forming (**5k**) (Table 4, entry 2).

Finally, in order to totally confirm the efficiency of the POLITAG-Pd(0)-L1 catalytic system in flow, a solution of phenol (**1a**) was continuously pumped for 25 h with no loss of efficiency and variation of selectivity. The flow set-up used in combination with our POLITAG-Pd(0)-L1 allows to convert over 100 mmol of phenolic compounds with only 0.5 mol% of Pd. This result is remarkable in comparison with both our batch protocol using POLITAG-Pd(0)-L1 and our previously reported flow protocol using Pd/C catalyst (1.1 mol%) [26].

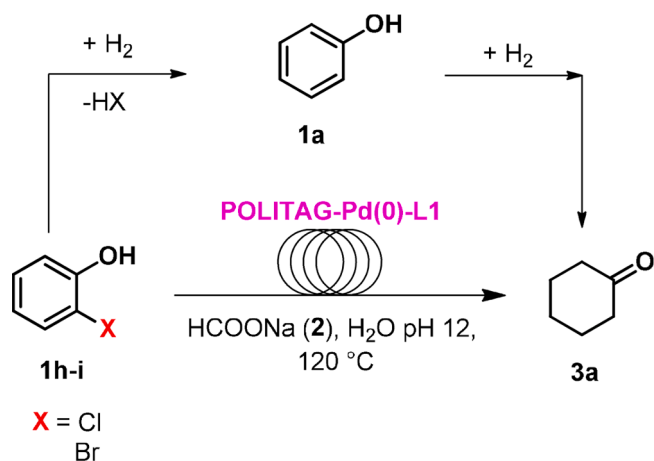
The POLITAG-Pd(0)-L1 catalyst employed for the conversion of over 100 mmol of different substrates was compared with the fresh catalytic system. TEM analyses show only a slight particle increase from 7.0 nm ± 3.3 nm to 11.1 nm ± 2.5 nm (Fig. 6). This evidence and the durability of our Pd-based heterogeneous catalyst highlight the importance of synergy between flow technology and tailor-made catalytic systems for an improved catalytic performance in hydrogen-transfer reactions.



Scheme 1. Proposed reaction mechanism for hydrogen-transfer reaction catalyzed by POLITAG-Pd(0)-L1.



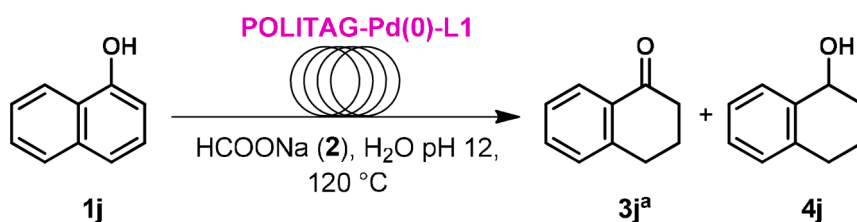
**Scheme 2.** Substrate scope for the hydrogenation of phenols in continuous flow conditions. <sup>a</sup>1h as starting material of 3a; <sup>b</sup> 1i as starting material of 3a.



**Scheme 3.** One-pot synthesis of cyclohexanone (**3a**) from *o*-halogenated phenols (**1h-i**).

#### 4. Conclusion

In conclusion **POLITAG-Pd(0)-L1** showed a good performance in terms of efficiency and selectivity in the hydrogenation of phenols to the corresponding cyclohexanone derivatives. The catalyst proved to be an effective water-tolerant heterogeneous catalyst while using sodium formate (**2**) as a safe hydrogen-source. The tailor-made architecture of the ionic tag designed for Pd nanoparticles immobilization, in combination with a flow technology procedure, reflected in an improved stability of the catalytic system that showed a very low metal leaching (0.01 ppm). With the same packed reactor representative more than 100 mmol of different substrates were converted with no loss in the chemical efficiency of the process. Satisfying selectivity have been obtained for differently substituted phenols while further study will be conducted to improve the conversion/selectivity ratio for more challenging variably substituted phenols.



Scheme 4. Continuous flow hydrogenation of 1-naphthol (1j). <sup>a</sup> Conversion=70%, 3j/4j=70/30.

### CRedit authorship contribution statement

**Valeria Trombettoni:** Investigation, Methodology, Writing – review & editing. **Francesco Ferlin:** Investigation, Methodology, Writing – review & editing. **Federica Valentini:** Investigation, Methodology, Writing – review & editing. **Filippo Campana:** Investigation, Writing – review & editing. **Matteo Silveti:** Investigation, Writing – review & editing. **Luigi Vaccaro:** Conceptualization, Methodology, Writing – review & editing.

### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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### Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.mcat.2021.111613](https://doi.org/10.1016/j.mcat.2021.111613).

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