

A Waste-Minimized Approach to Cassar-Heck Reaction Based on POLITAG-Pd⁰ Heterogeneous Catalyst and Recoverable Acetonitrile Azeotrope

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Three different Pd⁰-based heterogeneous catalysts were developed and tested in the Cassar-Heck reaction (i.e., copper-free Sonogashira reaction) aiming at the definition of a waste minimized protocol. The cross-linked polymeric supports used in this investigation were designed to be adequate for different reaction media and were decorated with different pincer-type ionic ligands having the role of stabilizing the formation and dimension of palladium nanoparticles. Among the ionic tags tested, bis-imidazolium showed the best performances in terms of efficiency and durability of the metal catalytic system. Eventually, aqueous acetonitrile azeotrope was selected as the

reaction medium as it allowed the best catalytic efficiency combined with easy recovery and reuse. Finally, the synergy between the selected catalyst and reaction medium allowed to obtain highly satisfactory isolated yields of a variety of substrates while using a low amount of metal catalyst. The high performance of the designed POLYmeric Ionic TAG (POLITAG)-Pd⁰, along with its good selectivity achieved in a copper-free process, also led to a simplified purification procedure allowing the minimization of the waste generated as also proven by the very low E-factor values (1.4–5) associated.

Introduction

The design of high-performance durable and reusable catalysts is one of the key challenges for aiming at a modern and more sustainable chemical production.^[1] Indeed, the replacement of stoichiometric reagents with small amounts of catalysts is crucial for the abatement of the waste generated in the preparation of target molecular architectures.^[2] In this context, transition metal-based heterogeneous catalytic systems play a crucial role: provided that they are truly recoverable and reusable in easily reproducible conditions, their easy separation from the reaction mixture can allow the minimization of waste

and also of the product metal contamination, facilitating the overall work-up/product isolation procedure.^[3] This is even more true if applied to the preparation of active pharmaceutical ingredients, which have highly stringent regulations on their metal contaminants.^[4]

Among the industrially used methodologies for the construction of C–C bond, Cassar-Heck or Sonogashira reactions are among the most studied since their first report in the literature in 1975. In fact, in the same year Heck^[5] and Cassar^[6] with a copper-free approach and Sonogashira^[7] using a combined palladium/copper catalysis disclosed separately different protocols allowing the possibility to form a new bond between a C(sp) (alkyne) with aromatic C(sp²).

The interest in the resultant alkynyl compounds has made these procedures widely important and investigated for the preparation of target pharmaceuticals or natural products.^[8] In the literature, there are reports dealing with the definition of environmentally friendly protocols for the preparation of alkynes and more in detail, to make Sonogashira and related reactions consistent with the current need of a more sustainable chemical production.^[9]

Among the strategies adopted, several studies aimed at the minimization of the palladium amount in combination with the use of a ligand under homogeneous conditions^[10] or by supporting the catalytic system on a heterogeneous support, aiming at its recovery and reuse.^[11]

Overall green efficiency of a protocol depends also on the use of the materials and solvents that directly influence the waste generation. These are utilized in large amounts in all the synthetic steps and especially at the purification stage.^[12] Therefore, the design and test of highly efficient heterogeneous

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Supporting information for this article is available on the WWW under <https://doi.org/10.1002/cssc.202101052>

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catalysts^[13] should consider the use of more sustainable media able to replace the most commonly used toxic solvents.^[9a,b,14]

Among the latter, a good option is offered by aqueous recoverable azeotropes that, being easily recoverable, can also be reused solving their dispersion and disposal issues.^[15] The possibility to recover the reaction medium is one of the key pillars to aim for a waste minimization also according to the EPA (Environmental Protection Agency) policies.^[16] Furthermore, the combination of an organic solvent with water can also be an effective tool to improve the process efficiency by increasing the combination of compounds soluble in different solvents.

Our continuous interest in the definition of waste-minimized procedures, is based on both the design of heterogeneous catalysts^[17] and use of green solvents,^[18] and with this aim we have developed our POLITAG-Pd⁰ (POLymeric Ionic-TAG) for a waste-minimized Cassar–Heck (copper-free Sonogashira) reaction.

We have previously proven that our crosslinked heterogeneous support decorated with pincer-type ionic tags is able to influence the palladium catalytic efficiency by stabilizing its nanoparticles^[17e] as well as its anionic Pd^{II} complexes.^[17a,d] By tuning the ligand architecture, our polymeric POLITAG support, and the reaction medium, we aim to regulate the reactivity and also the metal leaching. Taking into consideration these parameters, herein, we report a further example proving how important the catalyst design is in the development of environmentally friendly processes.

In this contribution we have reported that our catalyst system can reach a high performance in promoting the Cassar–Heck reaction by using a very low loading of Pd (0.01 mol%) in a recoverable acetonitrile–water azeotrope allowing different substrates to be processed. Moreover, the choice of this reaction medium and the optimization of work-up procedure has also led to a waste-minimized protocol as confirmed by the low E-factor^[19] values associated.

Results and Discussion

The cross-linked polymeric support developed by our group is a gel-type spaced rigid (SPACER, SP) crosslinked polystyrene resin obtained by suspension co-polymerization of equimolar

amounts of styrene and 4-vinylbenzyl chloride with 2% of 1,4-bis (4-vinylphenoxy)benzene as crosslinker,^[20] therefore featuring chlorinated anchoring centers, SP–Cl This support was designed considering the size and flexibility of the crosslinker in order to be efficient in various polar reaction media.

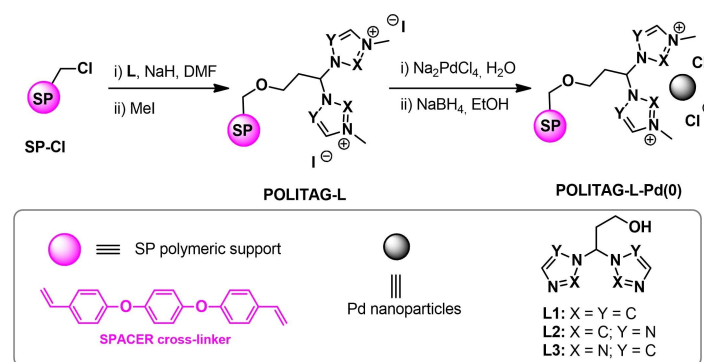
Functionalization followed the polymerization by anchoring one of the pincer-type ligands L1,^[17d] L2,^[17e] and L3^[17a] that after being subsequently quaternized, afforded three different POLITAGs supports (Scheme 1). The loading of supported ionic tags was determined by elemental analysis, and after palladium nanoparticles formed (Scheme 1) the corresponding POLITAGs–L–Pd⁰ heterogeneous catalysts could be achieved.

For the sake of an optimal comparison, we optimized the conditions in order to prepare the three different catalysts with comparable metal loadings (see Table S1 in the Supporting Information), as well as the size distribution of Pd nanoparticles for all the ionic tags employed as confirmed by transmission electron microscopy (TEM) analysis (see Figure S1 in the Supporting Information).

The difference of the ionic-tags was initially tested in terms of catalytic efficiency and nanoparticles stabilization of resultant POLITAGs–Pd⁰. The three catalysts were used in the Cassar–Heck reaction of representative iodobenzene (**1a**) and phenylacetylene (**2a**) at different reaction times, and then palladium leaching was measured after 4 h (Table 1).^[9h] 0.5 mol% of POLITAGs–Pd⁰ was used, together with DABCO (1,4-diazabicyclo [2.2.2]octane) as base and in γ -valerolactone (GVL) as reaction medium at 60 °C.

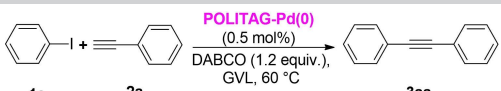
Although triazolium-based ionic tags L2 and L3 showed slightly higher catalytic efficiency after 2 h (Table 1, entries 3 and 5) the conversion at 4 h was comparable with the results obtained employing POLITAG-L1–Pd⁰ catalyst (Table 1, entries 2, 4, and 6). The latter showed the best compromise between catalytic performance and metal leaching and therefore was selected for the further progress of this study.

The reaction conditions for Cassar–Heck cross-coupling with POLITAG-L1–Pd⁰ were extended to different reaction media, and palladium leaching was always measured in all the solvents screened (Figure 1). As a result, it can be concluded that the catalyst efficiency was maintained in almost all the media tested while enormous differences in term of metal leached in solution could be observed. The most common dipolar aprotic solvents



Scheme 1. Schematic representation of POLITAG-L-Pd⁰ synthesis.

Table 1. Selection of POLITAG-Pd⁰.^[a]



Entry	Catalyst	t [h]	Conv. ^[b] [%]	Pd leaching ^[c] [ppm]
1	POLITAG-L1-Pd ⁰	2	90	26
2	POLITAG-L1-Pd ⁰	4	97	26
3	POLITAG-L2-Pd ⁰	2	96	128
4	POLITAG-L2-Pd ⁰	4	98	128
5	POLITAG-L3-Pd ⁰	2	96	83
6	POLITAG-L3-Pd ⁰	4	> 99	83

[a] Reaction conditions: POLITAG-Pd⁰ (0.5 mol%), **1a** (1 mmol), **2a** (1.5 equiv.), DABCO (1.2 equiv.), GVL (1 mL), 60 °C, 4 h. [b] Conversion was measured by GC analysis. The remaining materials were **1a** and **2a**. [c] Pd leaching was measured by MP-AES 4210 instrument.

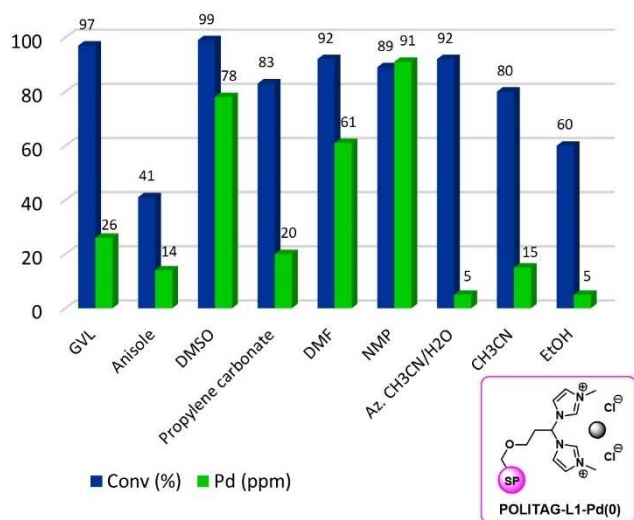


Figure 1. Conversion/leaching comparison for Cassar–Heck reaction between **1a** and **2a** using POLITAG-L1-Pd⁰ catalysts. Reaction conditions: POLITAG-L1-Pd⁰ (0.5 mol%), **1a** (1 mmol), **2a** (1.5 equiv.), DABCO (1.2 equiv.), solvent (1 mL), 60 °C, 4 h. Conversion was measured by GC analysis. The remaining materials were **1a** and **2a**. Pd leaching was measured by MP-AES 4210 instrument.

N,N-dimethylformamide (DMF), *N*-methyl-2-pyrrolidone (NMP), and dimethyl sulfoxide (DMSO) showed high conversion in product **3aa** with Pd leaching in the range of 61–91 ppm. These high values of metal were significantly decreased (from 26 to 5) when also more sustainable alternatives were used. On the base of these results, GVL, propylene carbonate, and CH₃CN/water azeotrope were selected for a further optimization.

The amount of POLITAG-L1-Pd⁰ catalyst was decreased in these sustainable reaction media by varying temperatures and times (see the Supporting Information, Table S2). Unfortunately, when 0.05 mol% of catalyst was employed, the conversion was low in propylene carbonate at 80 °C (12%, see the Supporting Information, Table S2, entry 4), while no product **3aa** at all was detected when 0.01 mol% of the catalyst was used (see the Supporting Information, Table S2, entry 9).

Under the same conditions, GVL gave better results affording **3aa** in 78 and 64%, with 0.05 and 0.01 mol% of POLITAG-L1-Pd⁰, respectively (see the Supporting Information, Table S2, entries 3 and 5). 80% conversion to **3aa** could be obtained by prolonging reaction time to 24 h (Supporting Information, Table S2, entry 8). The retained catalytic efficiency could be ascribable to the formation of solid precipitate, consisted in quaternized organic base, which make the reaction stirring difficult.

By plotting the conversion of **1a** for the selected reaction media when 0.01 mol% of POLITAG-L1-Pd⁰ is used (Figure 2), it is evident that the best catalyst performances were observed in aqueous acetonitrile azeotrope (Supporting Information, Table S2 entries 10–12). After further optimization of the process in this medium (base, temperature, and reaction time, Table S3) we could achieve full conversion to **3aa** after 7 h at 90 °C by using only 0.01 mol% of POLITAG-L1-Pd⁰ and DABCO as base (see Table S3, entry 7).

To have more details on the design of our catalyst and on the role of the support or the pincer-type ligand, we prepared and tested three different Pd⁰-based polymer supported catalysts (Figure 3), which differ in the support used in terms of rigidity and accessibility of catalytic sites and on the single imidazolium unit replacing the pincer-type unit.

Our bis-imidazolium ligand **L1** was immobilized on commercially available Janda Jel (a resin considered to act as flexible solvent-like system) and classic polystyrene Merrifield's featuring a smaller divinylbenzene as cross-linker. After the immobilization of Pd nanoparticles, JJ-L1-Pd⁰ and M-L1-Pd⁰ systems were prepared, respectively. Beside the fact that these catalysts showed fairly good conversions with our optimized reaction conditions, it is clearly visible how the nature of the crosslinker strongly influences the accessibility to the catalytic sites and ultimately not allows to quantitatively reach product **3aa**.

The catalyst obtained by immobilizing the single imidazolium unit onto our SPACER support led to SP-imi-Pd⁰, which showed a slightly better conversion in comparison with JJ-L1-Pd⁰ and M-L1-Pd⁰ confirming the higher efficiency achieved by

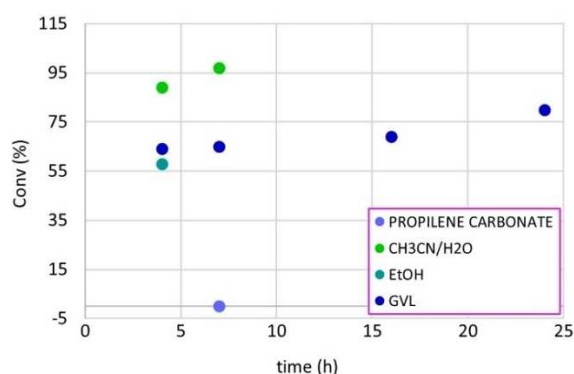


Figure 2. Conversion of **1a** into **3aa** during the time in the selected reaction medium using 0.01 mol% of POLITAG-L1-Pd⁰. Conversion was measured by GC analysis. The remaining materials were **1a** and **2a**. Reaction conditions: POLITAG-L1-Pd⁰ (9.4 wt%, 0.01 mol%, 0.117 mg), **1a** (1 mmol), **2a** (1.5 equiv.), DABCO (1.2 equiv.), 1 mL of medium, 80 °C.

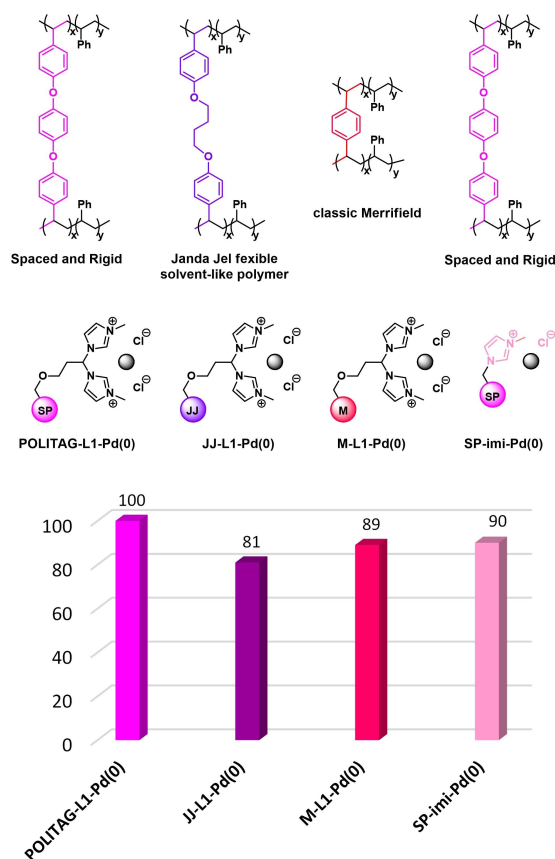


Figure 3. Comparison of catalytic performance between POLITAG-L1-Pd⁰ and other polymer-supported Pd⁰-based catalyst by changing support (JJ: Janda Jel; M: Merrifield) or ionic ligand (imi: imidazolium moiety). Reaction conditions: Pd⁰-catalyst (0.01 mol%), **1a** (1 mmol), **2a** (1.5 equiv.), DABCO (1.2 equiv.), 1 mL of CH₃CN/H₂O azeotrope, 90 °C, 7 h. Conversion was measured by GC analysis. The remaining materials were **1a** and **2a**.

combining the pincer-type ionic tag and our polymeric support to obtain the best results and the full conversion of **1a**.

Finally, the amount of POLITAG-L1-Pd⁰ was also tentatively decreased to 0.002 mol%, obtaining 87% conversion to **3aa** after 16 h. This result makes our system competitive, in terms of turnover number (TON) and frequency (TOF), with the best-performing Pd-NP-based heterogeneous catalysts reported in the literature (Table 2).

The protocol was finally optimized using 0.01 mol% of POLITAG-L1-Pd⁰, and a low Pd leaching (1 ppm) could be achieved (Supporting Information, Table S2, entry 12).

At the end of the process, the catalyst was filtered and washed with aqueous acetonitrile azeotrope. The latter could be recovered by distillation leading to a protocol with an overall E-factor value of 1.4 for the product **3aa**. This value is extremely low compared with some selected and best-performing protocols also using sustainable reaction media in the literature (Table 3). Although GVL,^[9h] N-hydroxyethylpyrrolidone (HEP),^[9b] and glycerol-based deep eutectic solvent (DES)^[9a] have been shown to be valid alternatives to toxic dipolar aprotic solvents by allowing high isolated yields and also being possibly recoverable,^[9a,b] they generally require an extraction work-up,

Table 2. Comparison of TON and TOF of POLITAG-L1-Pd⁰ with the best-performing Pd-NPs based catalysts for the representative coupling between **1a** and **2a**.

Pd [mol %]	Medium	t	TON	TOF (h ⁻¹)	Ref.
0.158	EtOH/H ₂ O	10 min	633	3750	[11a]
0.05	TPGS-750-M/H ₂ O	24 h	1900	79	[11e]
1.00	CH ₃ CN/H ₂ O (1:1)	10 min	100	600	[11d]
0.2	DMF	2 h	480	240	[11f]
0.005	CH ₃ CN	48 h	17200	358	[11g]
0.05	DMA	24 h	1760	73	[11i]
0.04	H ₂ O	0.5 h	2250	4500	[11j]
0.01	EtOH/H ₂ O (1:1)	24 h	9000	375	[11k]
0.06	H ₂ O	1 h	1583	1583	[11l]
0.01	H ₂ O	2 h	9600	4800	[11m]
0.05	ethylene glycol	2 h	1960	980	[11n]
0.002	az. CH ₃ CN/H ₂ O	16 h	43500	2806	this work

DMA = N,N-Dimethylacetamide

Table 3. Comparison of E-factor values in sustainable alternative reaction media for reaction between **1a** and **2a**.

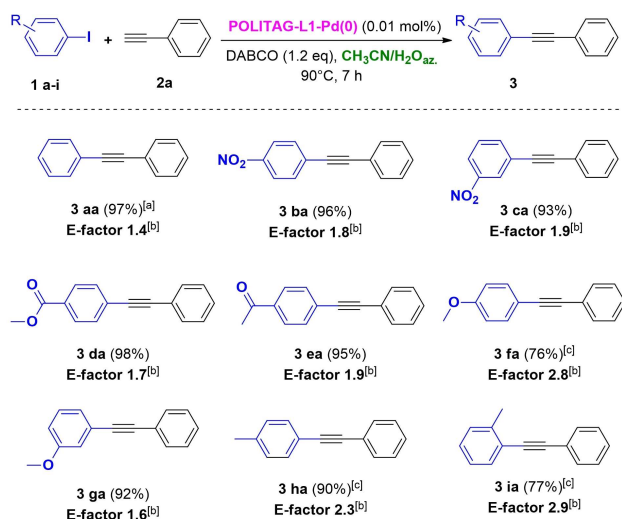
Reaction medium	3aa yield [%]	E-factor ^[a]	3aa Ref.
CH ₃ CN/H ₂ O az.	97	1.4	this work
CH ₃ CN/H ₂ O az.	77	17 ^[b]	[9g]
CH ₃ CN/H ₂ O az.	82	90 ^[c]	[9g]
GVL	70	73 ^[d]	[9h]
HEP	97	173	[9b]
DES	98	24.4 ^[e]	[9a]

[a] Calculated without considering product purification processes and recovered catalysts. [b] Heterogeneous base. [c] Homogeneous base. [d] Calculated considering 5 mL of petroleum ether and 3 × 1.5 mL of water for extraction as optimized by the same authors in ref. [9g]. [e] **1a** substituted with 3-chloriodobenzene.

which negatively influences the E-factor calculation. The use of a minimum-boiling-point azeotropic mixture allows an easy recovery accompanied with solvents and energy saving.^[15]

Moreover, the high catalyst efficiency and selectivity led us to improve the purification protocol. Filtration and washing of the solid reaction crude on silica pad with 10 mL of heptane affords the pure product **3aa** in 97% yield. The heptane used in purification step was then recovered in 94%. When the optimized conditions were scaled up to 10 mmol scale, similar results were obtained.

The optimized reaction conditions were efficiently extended to the Cassar–Heck coupling of different iodoarenes **1b–i** (Scheme 2) and **2a** in good to excellent isolated yields (76–98%). When electron-withdrawing substituted aryl iodides (**1b–e**) were employed, high yields were obtained by filtering and washing the reaction crude with toluene. The solvent used in this purification procedure was recovered in 97%. For deacti-



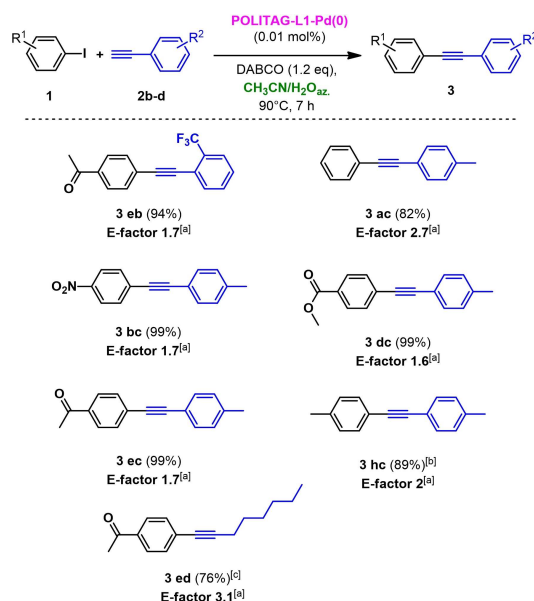
Scheme 2. Substrate scope for the Cassar–Heck reaction between iodoarene **1 a–i** and phenyl acetylene **2 a**. Reaction conditions: POLITAG-L1-Pd⁰ (9.4 wt %, 0.01 mol%, 0.117 mg), **1** (1 mmol), **2 a** (1.5 equiv.), DABCO (1.2 equiv.), 1 mL of CH₃CN/H₂O azeotrope, 90 °C, 7 h. Isolated yields are given in parentheses. [a] By conducting this reaction on 10 mmol scale, similar results were obtained. [b] E-factor calculated without considering purification process. [c] Reaction performed with 0.02 mol% of POLITAG-L1-Pd⁰ for 16 h.

vated substrates **1 f**, **1 h**, and **1 i** a slightly higher amount of POLITAG-L1-Pd⁰ was required together with 16 h of reaction time, and filtration with heptane was employed to isolate products.

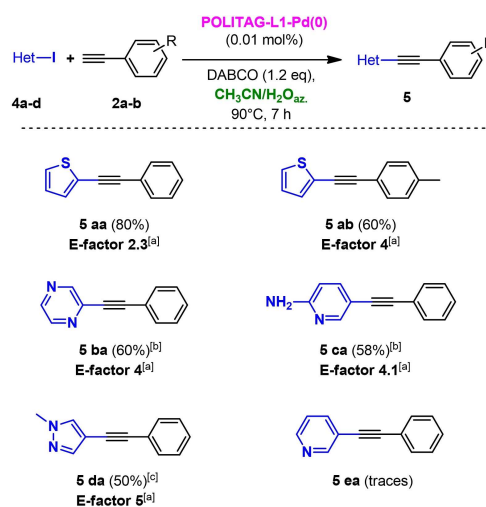
The optimized reaction conditions and purification protocol was revealed to be efficient also when different substituted phenyl acetylenes **2 b** and **c** (Scheme 3) were employed, as well as alkyl-substituted terminal alkyne **2 d**. The yields obtained for these substrates (76–99%) are comparable with the reactions performed with phenylacetylene **2 a** affording E-factor values in the range from 1.6 to 3.1, very good values also considering the most deactivated alkyne **2 d**.

The substrate scope was subsequently extended to different iodo-heterocycles **4 a–d** (Scheme 4) which are rarely investigated in this type of studies but are relevant to prove the generality of the protocol. 2-Iodothiophene **4 a** gave good isolated yields (60–80%) with our optimized reaction conditions when both phenylacetylene **2 a** and *p*-tolyl acetylene **2 b** were employed. When nitrogen-containing heterocycles were reacted with **2 a**, 0.02 or 0.03 mol% of POLITAG-L1-Pd⁰ was required to satisfactorily afford the products **5 ba**, **5 ca**, and **5 da**. Product **5 ca**, which contains an amino group, was successfully isolated by recrystallization. However, in these reaction conditions 3-iodopyridine **5 e** gave the desired product only in traces. It is worthy to note that the protocol here developed showed good efficiency in terms of waste minimization (E-factor range 3–27) even by including in the calculation the amount of materials used for purification (solvents and SiO₂) (see the Supporting Information for further details).

As an illustration of the applicability of our protocol in the synthesis of API, we conducted the Cassar–Heck coupling with our POLITAG-L1-Pd⁰ for the synthesis of Eniluracil intermediate

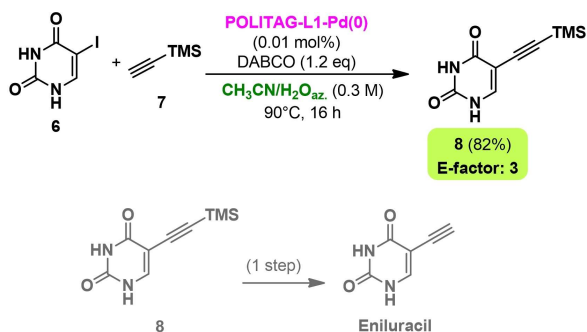


Scheme 3. Substrate scope for the Cassar–Heck reaction between iodoarene **1** and phenyl acetylene **2 b–d**. Reaction conditions: POLITAG-L1-Pd⁰ (9.4 wt %, 0.01 mol%, 0.117 mg), **1** (1 mmol), **2** (1.5 equiv.), DABCO (1.2 equiv.), 1 mL of CH₃CN/H₂O azeotrope, 90 °C, 7 h. Isolated yields are given in parentheses. [a] E-factor calculated without considering purification process. [b] Reaction performed with 0.03 mol% of POLITAG-L1-Pd⁰ for 16 h. [c] Reaction performed with 0.02 mol% of POLITAG-L1-Pd⁰ for 24 h.



Scheme 4. Substrate scope for the Cassar–Heck reaction between iodo-heterocycles **4 a–d** and phenyl acetylenes **2 a** and **b**. Reaction conditions: POLITAG-L1-Pd⁰ (9.4 wt %, 0.01 mol%, 0.117 mg), **1** (1 mmol), **2** (1.5 equiv.), DABCO (1.2 equiv.), 1 mL of CH₃CN/H₂O azeotrope, 90 °C, 7 h. Isolated yields are given in parentheses. [a] E-factor calculated without considering purification process. [b] Reaction performed with 0.02 mol% of POLITAG-L1-Pd⁰ for 16 h. [c] Reaction performed with 0.03 mol% of POLITAG-L1-Pd⁰ for 16 h.

(**8**) (Scheme 5). Eniluracil is an inactivator of the enzyme dihydropyrimidine dehydrogenase obtained by the coupling of 5-iodouracil (**6**) and trimethylsilyl acetylene (**7**) with subsequent deprotection to remove trimethylsilyl group.^[8g]



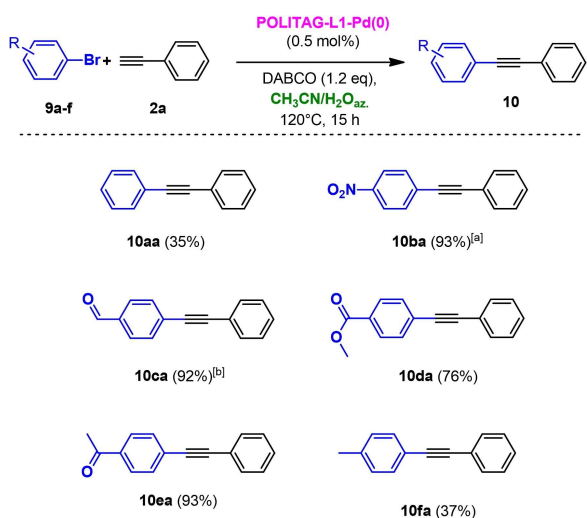
Scheme 5. Synthesis of Eniluracil intermediate (**8**) by Cassar–Heck reaction between 5-iodouracil (**6**) and trimethylsilylacetylene (**7**) with POLITAG-L1-Pd⁰. Isolated yield is given in parentheses. Reaction conditions: POLITAG-L1-Pd⁰ (0.01 mol%), **6** (1 mmol), **7** (1.5 equiv.), DABCO (1.2 equiv.), 3 mL of CH₃CN/H₂O azeotrope, 90 °C, 16 h.

We found optimal solubility of the starting material **6** in our selected aqueous acetonitrile azeotrope reaction medium, which allowed us to obtain high conversion in product **8** with only 0.01 mol% of POLITAG-L1-Pd⁰.

Interestingly, once the catalyst was separated by hot filtration, the product **8** precipitated in the reaction mixture at room temperature and could be easily obtained by filtration. This optimized protocol led to an isolated yield of 82% and an E-factor value of 3.

Notably, the use of aryl iodide is also widely exploited in pharmaceutical industries. This choice is generally related to the interest in developing highly efficient processes. We decided to also perform the Cassar–Heck reaction with generally less-reactive aryl bromides (Scheme 6).

With the selected POLITAG-L1-Pd⁰ catalyst and CH₃CN aqueous azeotrope as reaction medium, we were able to obtain



Scheme 6. Substrate scope for the Cassar–Heck reaction with aryl bromide **6**. Reaction conditions: POLITAG-L1-Pd⁰ (9.4 wt%, 0.5 mol%, 5.66 mg), **9** (1 mmol), **2** (1.5 equiv.), DABCO (1.2 equiv.), 1 mL of CH₃CN/H₂O azeotrope, 120 °C, 15 h. Isolated yields are given in parentheses. [a] Reaction performed with 0.01 mol%. [b] Reaction conducted in 8 h.

good isolated yields for electron-withdrawing aryl bromides (**9b–d**); while poor yields were observed with deactivated 4-bromotoluene (**6e**) as well as with bromobenzene (**9a**) under the same reaction conditions.

Conclusion

Three different POLITAG-L1-Pd⁰ have been developed and tested in the Cassar–Heck reaction. Among the ionic tags screened, bis-imidazolium pincer-type ligand **L1** was selected for giving the higher stabilization of Pd nanoparticles on polymeric support in comparison with triazolium based counterparts **L2** and **L3**. Our polymeric support featuring a rigid and spaced structure due to the cross-linker used (SPACER) plays a crucial role in the overall efficiency of the Pd⁰ system especially if compared to catalysts obtained from commercially available supports (JJ-L1-Pd⁰, M-L1-Pd⁰). Aqueous acetonitrile azeotrope has been identified as the best reaction medium to perform the coupling with very low Pd amount (0.002 mol%). With these conditions high turnover number (TON) and frequency (TOF) values were measured (43500 and 2806 h^{−1} respectively). The optimized reaction conditions were selected to have the best match between low catalyst amount (0.01 mol%) and reaction time (7 h). These conditions allowed us to synthesize a wide variety of alkynyl products with isolated yields ranging from good to excellent values.

Moreover, the synergy between the reaction medium selected and high catalyst performance and selectivity led to an effective and simple purification that allowed us to achieve a minimal-waste production; in fact, low E-factor values have been calculated in the range from 1.4 to 5 and from 3 to 27 if also purification materials were considered. Our optimized protocol was extended also to the synthesis of Eniluracil intermediate with good isolated yield and low E-factor value. Finally, the efficiency of our POLITAG-L1-Pd⁰ in the selected reaction medium has been proved by employing generally less reactive aryl bromides.

Experimental Section

Unless otherwise stated, all chemicals were purchased and used without any further purification. GLC analyses were performed by using Hewlett-Packard HP 5890 SERIES II equipped with a capillary column DB-5MS (30 m, 0.32 mm), a flame ionization detector (FID), and helium as gas carrier. GC-EIMS analyses were carried out by using a Hewlett-Packard HP 6890 N Network GC system/5975 mass selective detector equipped with an electron impact ionizer at 70 eV. Melting points were measured on a Büchi 510 apparatus. NMR spectra were recorded on a Bruker DRX-ADVANCE 400 MHz (¹H at 400 MHz, ¹³C at 100.6 MHz and ¹⁹F at 376.4 MHz) in CDCl₃. Chemical shifts are reported in ppm (δ), coupling constant (*J*) in Hertz, and multiplicity are reported as follows: s = singlet, bs = broad singlet, d = doublet, dd = double doublet, td = double triplet, t = triplet, m = multiplet. Elemental analysis (EA) was conducted on Elementar UNICUBE[®] elemental analyzer. Metal loading was measured using MP-AES 4210 instrument. Products purification was performed through filtration on silica plug using 230–400 mesh silica gel. 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.

General procedure for Cassar–Heck reaction

A 2 mL screw capped vial, equipped with a magnetic stirrer, was charged with the aryl halide (1 mmol), the terminal alkyne (1.5 equiv.), DABCO (1.2 equiv.), catalyst POLITAG-L1-Pd⁰ (9.4 wt%, 0.117 mg, 0.01 mmol%), and 1 mL of CH₃CN/H₂O azeotrope (1 M, 84:16 w/w). The reaction mixture was then stirred at 90 °C for 7 h. The conversion was determined by GLC analyses. After reaction completion, the catalyst was separated through filtration on 0.45 μm filter and washed with 1 mL of CH₃CN/H₂O azeotrope, which was then recovered through distillation (95% azeotrope recovered).

Work-up with heptane (method A)

The product was isolated through filtration and washing on silica plug (500 mg) using heptane (5 mL). The solvent was recovered at 94% through distillation.

Work-up with toluene (method B)

The product was isolated through filtration and washing on silica plug (150 mg) using toluene (5 mL). The solvent was recovered at 97% through distillation.

General procedure for leaching determination

After reaction completion, the catalyst was separated through filtration and washed with 1 mL of CH₃CN/H₂O azeotrope. The reaction mixture was dried under vacuum, dissolved in 2 mL of aqua regia, and stirred for 1 h at room temperature. The reaction mixture was transferred in a 10 mL graduated flask and Milli-Q water was added to reach the final volume. If present, residual solid was filtered off and the sample was analyzed by MP-AES 4210 instrument.

Acknowledgements

The Università degli Studi di Perugia and MIUR are acknowledged for financial support for the project AMIS, through the program "Dipartimenti di Eccellenza-2018-2022".

Sterling SpA is acknowledged for useful discussion on the synthesis of target APIs. Open Access Funding provided by Politecnico di Milano within the CRUI-CARE Agreement.

Conflict of Interest

The authors declare no conflict of interest.

Keywords: azeotrope · C–C coupling · Cassar–Heck · polymer-supported catalyst · waste minimization

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Manuscript received: May 19, 2021
Revised manuscript received: July 1, 2021
Accepted manuscript online: July 9, 2021
Version of record online: July 22, 2021