

Impregnated palladium on magnetite as a watercompatible catalyst for the cycloisomerization of alkynoic acid derivatives †

Beatriz Saavedra,^a Juana M. Pérez,^a María J. Rodríguez-Álvarez,^b Joaquín García-Álvarez^{*b} and Diego J. Ramón^{*a}

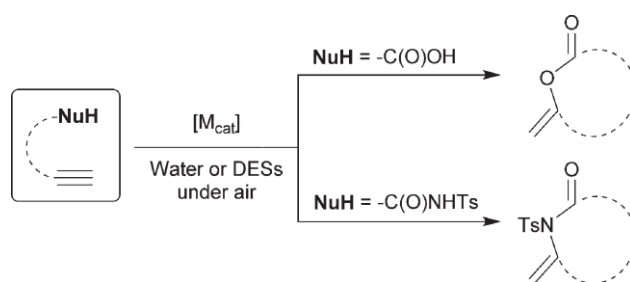
This work describes the catalytic activity of palladium(II) species in the cycloisomerization of alkynoic acids and their derivatives in aqueous media as well as in Deep Eutectic Solvents (DESs), with one of the lowest metal catalyst loadings reported so far in the literature. Different substrates such as terminal and internal alkynes or alkynyl sulfonylimides were studied, obtaining selectivity either to the cyclic compound or the hydrolysed keto derivative. This new system avoids the use of harmful solvents and employs very efficient and recoverable heterogeneous catalysts.

Introduction

Cycloisomerization processes¹ are amongst the most valuable transformations according to the *principles of green chemistry*,² since they show the highest atom and step economy.³ The metal-catalyzed intramolecular cycloaddition of heteroatomic nucleophiles to an alkyne is a straightforward and highly selective method for the synthesis of heterocyclic products, which usually present an increased structural complexity when compared with their acyclic starting materials (Scheme 1).¹ Some of the crucial points to bear in mind when designing *catalytic green chemical processes* involve: (i) the use of safe, nontoxic,

cheap and sustainable solvents [like water and Deep Eutectic Solvents (DESs)];^{4,5} (ii) the absence of co-catalysts (usually bases, acids or halogen abstractors are employed); and (iii) the use of aerobic conditions (without a protecting atmosphere).

Over the years, numerous protocols for the cycloisomerization of alkynoic acid derivatives catalyzed by transition metals have been reported, giving rise to a reliable and forthright synthetic tool for the production of highly substituted cyclic enol-lactones,^{6,7} with palladium species being the most used catalyst. Although homogeneous⁶ catalysts were initially used, there are some examples in the literature which used hetero-



Scheme 1 Metal-catalyzed cycloisomerization of alkynoic acids or alkynyl sulfonylimides using sustainable solvents as reaction media in the presence of air.

geneous palladium catalysts.⁷ However, most of these catalysts required: (i) protocols with high catalyst loadings; (ii) additives (such as co-catalysts or bases); and (iii) the use of volatile organic solvents. Thus, only a few catalytic systems were able to carry out the cycloisomerization of alkynoic acid derivatives using sustainable solvents.⁸

On the other hand, the utilization of heterogeneous catalysts in organic synthesis presents important and obvious advantages including easy isolation and possible recycling, among others.⁹ In this sense, magnetite¹⁰ used as a support is particularly attractive since its magnetic properties allow easy separation of the catalyst from the reaction mixture, just using an external magnet (magnetic decantation) without the need for tedious, time-consuming and waste-production steps (filtration, centrifugation or membrane separation steps). These unique properties make magnetite an excellent support for many different metallic catalysts.¹¹

With all these precedents in mind, herein we report a simple and heterogeneous catalyst based on palladium(II)

oxide nanoparticles supported on magnetite for the cycloisomerization of alkynoic acid derivatives in aqueous media or Deep Eutectic Solvents (DESs). It is important to note that: (i) a higher activity is achieved by using palladium(II) oxide impregnated on magnetite as a catalyst; (ii) the reactions proceed in water or DES under aerobic conditions and without the assistance of any co-catalyst, and (iii) the use of water as a reaction medium allows the catalyst recycling (up to 4 consecutive times) without loss of catalytic activity or selectivity.

Results and discussion

To start with this study, the cycloisomerization reaction was evaluated using palladium(II) oxide impregnated on magnetite as a catalyst and commercially available 4-pentynoic acid (1a) as the model for the reaction condition optimization (Table 1).

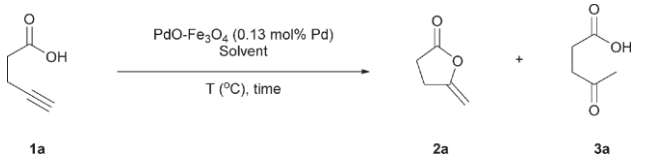
Initially, the reaction was performed using different DESs as sustainable solvents (Table 1, entries 1–12), obtaining the best result with the choline chloride-based eutectic mixture [ChCl : urea/1 : 2] (entry 7).¹² When the reaction was carried out in pure water as a solvent (entries 13–31) the yield was substantially improved even at room temperature (entry 14). Then, a study on the evolution of the reaction was carried out at different temperatures (see ESI†). The ketoacid 3a was obtained as a minor product of the tandem process cycloisomerization/hydrolysis after 4 days at room temperature (entry 20). Compound 3a was the only product obtained after 7 days at room temperature (entry 21), 4 days at 50 °C (entry 25) or 7 h at 90 °C (entry 31). These results showed the selectivity of the catalyst, capable of performing regioselectively the 5-*exo*-dig cyclization with no hydrolysis.

It should be also pointed out that the complete hydrolysis of the previously isolated compound 2a to the ketoacid 3a took place after 17 h in water at 90 °C in the absence of impregnated palladium on magnetite as a catalyst, while in the presence of the catalyst the whole process took only 7 h (compare with entry 31). These experiments showed that the impregnated palladium on magnetite catalyst also catalyzed the final hydrolysis. Moreover, an increase of the temperature enhanced the reaction rate, obtaining the enol-lactone 2a in 60 min at room temperature (entry 14), in 30 min at 50 °C (entry 23), or only in 10 min at 90 °C (entry 27).

At this point, it should be highlighted that this reaction time is one of the lowest reported so far in the literature⁸ for this cycloisomerization process in sustainable solvents.

Once the optimal conditions were determined (entry 27 in Table 1 or entry 1 in Table 2), other catalysts were tested in the model catalytic reaction (Table 2). Prior to these studies we proved that the reaction without catalyst failed in the aforementioned optimized reaction conditions (entry 2). For completeness of the possible blank experiments, we also evaluated the activity of the magnetite support on its own. Nanoparticles or microparticles of magnetite were used as catalysts with the results showing the inactivity of the support (entries 3 and 4).

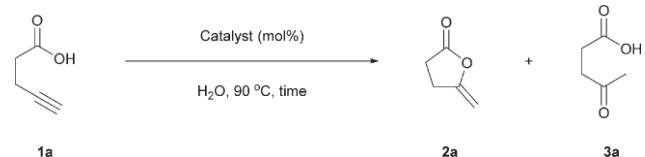
Table 1 Optimization of the reaction conditions^a



Entry	Solvent	T (°C)	Time	2a ^b (%)	3a ^b (%)
1	ChCl : urea (1 : 2)	25	45 min	0	0
2	ChCl : glycerol (1 : 2)	25	45 min	2	0
3	ChCl : ethylene glycol (1 : 2)	25	45 min	3	0
4	AcChCl : urea (1 : 2) ^c	25	45 min	2	0
5	ChCl : resorcinol (1 : 1)	25	45 min	30	0
6	ChCl : acetamide (1 : 2)	25	45 min	5	0
7	ChCl : urea (1 : 2)	90	10 min	81	0
8	ChCl : glycerol (1 : 2)	90	10 min	32	0
9	ChCl : ethylene glycol (1 : 2)	90	10 min	36	0
10	AcChCl : urea (1 : 2)	90	10 min	67	0
11	ChCl : resorcinol (1 : 1)	90	10 min	65	0
12	ChCl : acetamide (1 : 2)	90	10 min	25	0
13	H ₂ O	25	30 min	37	0
14	H ₂ O	25	60 min	100	0
15	H ₂ O	25	90 min	100	0
16	H ₂ O	25	2 h	100	0
17	H ₂ O	25	4 h	100	0
18	H ₂ O	25	1 d	92	8
19	H ₂ O	25	2 d	93	7
20	H ₂ O	25	4 d	67	33
21	H ₂ O	25	7 d	0	100
22	H ₂ O	50	10 min	67	0
23	H ₂ O	50	30 min	100	0
24	H ₂ O	50	2 h	100	0
25	H ₂ O	50	4 d	0	100
26	H ₂ O	90	5 min	90	0
27	H ₂ O	90	10 min	100	0
28	H ₂ O	90	30 min	100	0
29	H ₂ O	90	60 min	100	0
30	H ₂ O	90	2 h	73	27
31	H ₂ O	90	7 h	0	100

^a Reaction carried out using compound 1a (0.1 mmol) and 0.5 mg of catalyst (0.13 mol% Pd) in 0.2 mL of solvent. ^b Conversion determined by GC using tridecane as an internal standard. ^c AcChCl (acetylcholine chloride).

After the non-activity of magnetite was tested, different metal oxides impregnated on magnetite (entries 5–16) were evaluated as catalyst, observing that only PtO/Pt₂O–Fe₃O₄ and PdO/Cu–Fe₃O₄ showed some catalytic activity (entries 5 and 16). However, the selectivity was poor, since the ketoacid 3a was detected. Once palladium was found to be the most active metal, other commercially available palladium species were tested (being either homogeneous or heterogeneous catalysts) under the previously optimized catalytic conditions (water at 90 °C). In all the palladium catalyst tests, the amount of loading required to obtain a complete conversion was higher than that using magnetite as a support (compare entries 1, 17, 19, 21, 23 and 25), thus highlighting the superior catalytic activity of the magnetite-based palladium catalyst. At lower reaction times, the obtained yield was not quantitative: for instance, PdO·H₂O (1.42 mol%) or Pd(MeCN)₂Cl₂ (0.1 mol%) gave product 2a in 71 or 89% yield, respectively, after 5 min.

Table 2 Optimization of the catalyst^a


Entry	Catalyst	Time	2a ^b (%)	3a ^b (%)
1	PdO-Fe ₃ O ₄ (0.13)	10 min	100	0
2	—	10 min	0	0
3	Nano-Fe ₃ O ₄ (6.48)	10 min	0	0
4	Micro-Fe ₃ O ₄ (6.48)	10 min	0	0
5	PtO/Pt ₂ O-Fe ₃ O ₄ (0.13)	10 min	40	7
6	Au ₂ O ₃ -Fe ₃ O ₄ (0.13)	10 min	0	0
7	Cu/CuO-Fe ₃ O ₄ (0.13)	10 min	0	0
8	Ru ₂ O ₃ -Fe ₃ O ₄ (0.13)	10 min	0	0
9	IrO ₂ -Fe ₃ O ₄ (0.13)	10 min	0	0
10	CoO-Fe ₃ O ₄ (0.13)	10 min	0	0
11	NiO-Fe ₃ O ₄ (0.13)	10 min	0	0
12	Rh ₂ O ₃ -Fe ₃ O ₄ (0.13)	10 min	0	0
13	Ag ₂ O/Ag-Fe ₃ O ₄ (0.13)	10 min	0	0
14	OsO ₂ /OsO ₂ (OH) ₂ -Fe ₃ O ₄ (0.13)	10 min	0	0
15	NiO/Cu-Fe ₃ O ₄ (0.19/0.22)	10 min	0	0
16	PdO/Cu-Fe ₃ O ₄ (0.17/0.13)	10 min	76	22
17	Pd/C (1.18)	10 min	100	0
18	Pd/C (1.10)	7 h	70	30
19	PdO·H ₂ O (1.85)	10 min	100	0
20	PdO·H ₂ O (2.06)	7 h	0	100
21	PdCl ₂ (3.87)	10 min	100	0
22	PdCl ₂ (4.05)	7 h	0	100
23	Pd(AcO) ₂ (0.10)	10 min	100	0
24	Pd(AcO) ₂ (0.10)	7 h	100	0
25	Pd(MeCN) ₂ Cl ₂ (0.10)	10 min	100	0
26	Pd(MeCN) ₂ Cl ₂ (0.10)	7 h	100	0

^a Reaction carried out using compound 1a (0.1 mmol) in 0.2 mL of solvent. ^b Conversion determined by GC using tridecane as an internal standard.

Moreover, standard palladium homogeneous catalysts like Pd(AcO)₂ or Pd(MeCN)₂Cl₂ were unable to promote the hydrolysis reaction at longer reaction times, recovering quantitatively the compound 2a unchanged (Table 2, entries 24 and 26).

Once the best catalytic settings were established (in terms of catalyst and reaction conditions), the scope of this catalytic transformation was evaluated (Table 3). The magnetite-impregnated Pd catalyst showed a wide applicability and tolerance to functional groups at α position of the acid function with one of the lowest metal catalyst loadings reported.^{7,8} Lower temperatures (50 °C) were required when aliphatic substituents were attached at that position (entry 3) in order to perform the reaction selectively. The influence of the length of the aliphatic chain was also studied; when a methylene unit was added to alkyne acid, the cycloisomerization process became slower, compared with the final hydrolysis, obtaining only a small amount of 2c (detected by GC), with the ketoacid 3c being the main product (entry 5). As previously observed for other catalytic systems,^{7,8} alkyne acids containing longer aliphatic chains ($n = 3$) were inactive towards cycloisomerization (entry 6). Once the length of the alkyl chain was discovered as a crucial parameter, the relative position of the triple C–C bond

was also evaluated. Thus, the reaction using a highly challenging internal alkyne acid gave the expected cyclic compound 2e with an excellent result (entry 7), although the reaction time must be increased. This observed experimental fact is consistent with the *trans* addition of the acid/imide group on the alkyne, which is activated by π -coordination to Pd. It should also be pointed out that for this internal alkyne: (i) the addition was regioselective, since only Z-product is detected in

the crude mixture; and (ii) no traces of the corresponding 6-membered ring, resulting from an *endo* instead of an *exo* cyclization, were detected, thus providing a new insight into the high selectivity of the catalytic system. As expected, the corresponding ketoacid 3e was obtained just by increasing the reaction time (entry 8). After the good results obtained for the cycloisomerization of alkyne acids in water, we decided to focus our attention on the cycloisomerization of alkyne sulfonylimides, in which the intramolecular addition of a N–H bond across the carbon–carbon triple bond facilitates the formation of the corresponding alkylidene lactams (Scheme 1).^{6p,13} Cycloisomerization of alkyne imides is usually more challenging than that of their corresponding carboxylic acid counterparts as typically it demands the use of organic solvents as the reaction media. Thus, there are really few examples in the literature which describe the cycloisomerization of alkyne imides in water and under aerobic conditions.^{8j,n} Bearing in mind the mentioned precedents, we observed that the magnetite-impregnated Pd catalyst also proved to be compatible with *N*-tosyl derivatives (entries 9–15, Table 3). Cyclization of 2f (entry 9) proceeds so slowly in comparison with the hydrolysis reaction (entry 10) that only 30% of compound 2f could be isolated after 8 h, with the starting reagent and keto derivative 3f being detected in the crude mixture. Functional groups such as ester (entries 11 and 14) or allyl (entry 13) were compatible with the cyclization, showing that in these cases the process was totally selective.

Finally, most of the substrates (either cyclic lactones or lactams) underwent successfully the hydrolysis reaction, giving rise to the corresponding keto acids or imides (entries 2, 4, 5, 8, 10 and 12). However, when the bulkiness of substitution at α position was increased, the corresponding hydrolysis products were not observed (entries 13–15).

Taking into account the following noteworthy catalytic features: (i) the aforementioned higher activity of the impregnated palladium on magnetite in the cycloisomerization of compound 1a, (ii) the possibility of reusing the aqueous reaction media in further transformations,¹⁴ and (iii) the easy catalyst recycling (just using an external magnet) after its use,¹⁵ we decided to study the recyclability of our catalytic system (Fig. 1), which is considered to be a crucial point in the direction of *sustainable chemistry* for many industrial processes.¹⁵

For this purpose, after the completion of the reaction, the mixture was extracted with ethyl acetate in order to remove all organic compounds, and the mixture of water and catalyst was reused under the same reaction conditions. Taking advantage of the magnetic properties of our catalyst we also investigated its recovery by magnetic decantation and fresh solvent was

Table 3 Scope of the cyclization of alkynoic acids and derivatives by PdO–Fe₃O₄

Entry ^a	R ¹	R ²	R ³	X–Z	n	Time	Product	Yield ^b (%)
1	H	H	H	O	1	10 min	2a	100 ^c
2	H	H	H	O	1	7 h	3a	100
3	Me	Me	H	O	1	1 d	2b	55 ^d
4	Me	Me	H	O	1	1 d	3b	92
5	H	H	H	O	2	45 h	3c	98
6	H	H	H	O	3	3 d	3d	0 ^e
7	H	H	Ph	O	1	1 d	2e	96
8	H	H	Ph	O	1	4 d	3e	75
9	H	H	H	N-Ts	1	8 h	2f	30 ^f
10	H	H	H	N-Ts	1	1 d	3f	95
11	CO ₂ Me	H	H	N-Ts	1	5 h	2g	95 ^g
12	CO ₂ Me	H	H	N-Ts	1	2 d	3g	83
13	CO ₂ Me	Allyl	H	N-Ts	1	2 d	2h	97
14	CO ₂ Et	Me	H	N-Ts	1	5 h	2i	95 ^g
15	CO ₂ Et	Me	Et	N-Ts	1	4 d	2j	76

^a Reaction carried out using compounds 1a–j (0.1 mmol) and 0.5 mg of catalyst (0.13 mol% Pd) in 0.2 mL of solvent. ^b Isolated yield. ^c Yield determined by GC using an internal standard. ^d Reaction carried out at 25 °C. ^e The starting compound 1d was recovered unchanged. ^f 25% of 3f and 40% of the starting compound 1f were detected by ¹H NMR of crude mixture. ^g Reaction carried out at 50 °C.

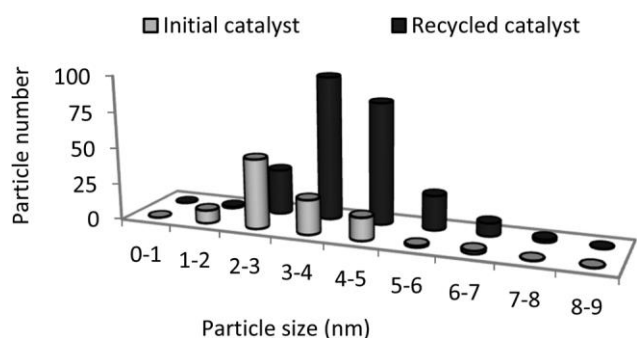
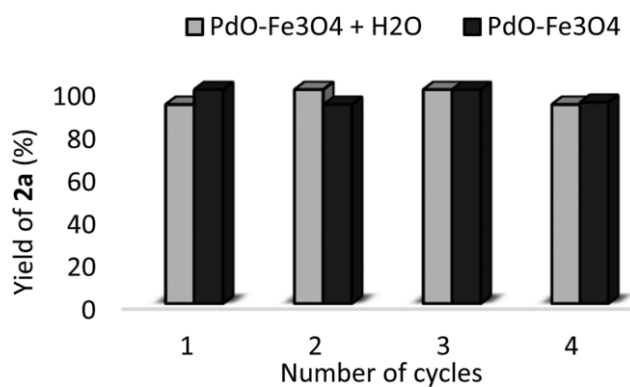
Fig. 1 Recyclability of PdO–Fe₃O₄ + H₂O and PdO–Fe₃O₄.

Fig. 2 Particle size distribution of fresh and recycled catalysts.

used. In both cases, the catalytic system could be recycled up to 4 consecutive times without any decrease in catalytic activity or selectivity.

In order to study the heterogeneity of the reaction, a simple hot-filtration experiment was carried out. Thus, a cycloisomerization reaction of 1e was performed under standard conditions and after 5 h the catalyst was recovered by magnetic decantation and the alkynoic acid 1a was added to the homogeneous solution. After 10 minutes at 90 °C, the GC analysis of the crude mixture showed the presence of compounds 2e (40%) and 2a (37%). This experimental result seems to indicate that a partial leaching of the active species from the surface of the catalyst to the water solution occurs.

The nanosize distribution of the palladium heterogeneous catalyst was measured after the recycling process (Fig. 2). The particle size distribution showed a small overall increase, observing that, after the reaction, nanoparticles tend to sinter,

giving a mean value of 4.0 ± 1.1 nm in comparison with the initial mean value of 3.1 ± 1.0 nm.

Furthermore, ICP-MS analysis of the solution after the catalytic reaction showed leaching of a small amount of palladium (7.1% of the initial amount) and iron (0.1% of the initial amount), which is in accordance with the results obtained in the hot-filtration experiment. Other experiments were carried out in order to study palladium leaching. When Pd/C was employed as a catalyst under optimized conditions the ICP-MS analysis of the water solution showed a similar leaching of palladium in comparison with PdO–Fe₃O₄ (6.4% of the initial amount). However, no leaching of palladium was observed when PdO–Fe₃O₄ was treated with either an acid (butyric acid) and alkyne (1-hexyne) substrate (proportion 1 : 1) in water or only in the presence of water at 90 °C.

XPS analysis was performed to confirm the oxidation state of the catalyst after the catalytic reactions. Thus, this analysis showed that a portion of the initial palladium(II) is oxidized to palladium(IV), but this slightly modification seemed not to change the initial activity of the catalyst (Fig. 3).

Finally, to prove the applicability of the process, the model reaction was performed on a gram-scale (Scheme 2). This reaction, performed with 4-pentynoic acid **1a** (10 mmol) in 20 mL of water as a solvent, was stirred at 90 °C for 7 hours, cooled to room temperature and extracted with 2-MeTHF (5 mL), a potential sustainable alternative solvent. The organic phase was evaporated to dryness and analysed by ¹H NMR (see ESI†) to afford 1.07 g of pure product **3a** (92% yield) without the need for chromatography purification.

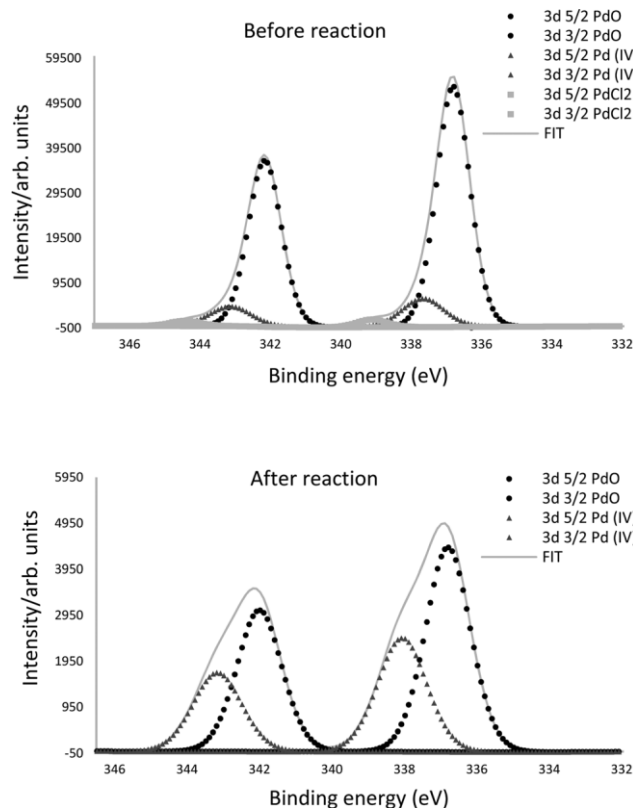
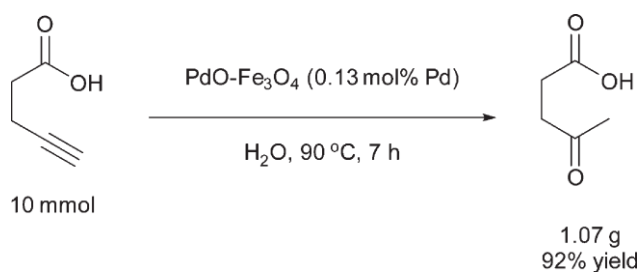


Fig. 3 XPS of fresh and recycled palladium catalysts.



Scheme 2 Gram-scale reaction. Isolated product **3a** in 92% yield without chromatography purification.

Experimental

General

Solvents and reagents were used as obtained from commercial sources without further purification. ¹H NMR (300 MHz) spectra were recorded on a Bruker AC-300 NMR spectrometer in the proton coupled mode. ¹³C NMR (75.5 MHz) spectra were recorded on a Bruker AC-300 NMR spectrometer in the proton decoupled mode at 20 °C; chemical shifts are given in δ (parts per million) and coupling constants (J) in hertz. Low-resolution mass spectra (EI) were recorded at 70 eV on an Agilent Technologies GC/MS-5973N spectrometer or an Agilent 5973 Network spectrometer with a Direct Insertion Probe (73DIP-1), giving fragment ions in m/z with relative intensities (%) in parentheses. High-resolution mass spectra (EI) were recorded at 70

eV on an Agilent 7200 flight (Q-TOF) spectrometer with a Direct Insertion Probe (73DIP-1), giving fragment ions in m/z with relative intensities (%) in parentheses. Infrared spectra were measured on a Jasco FT/IR-4100 Fourier Transform Infrared Spectrometer. Melting points were obtained with a Reichert Thermovar apparatus. XPS analyses were carried out using a VG-Microtech Mutilab. TEM images were obtained using a JEOL model JEM-2010 instrument equipped with an X-ray detector, OXFORD INCA Energy TEM 100, for microanalysis (EDS). XRF analyses were performed using a PHILIPS MAGIX PRO (PW2400) X-ray spectrometer equipped with a rhodium X-ray tube and a beryllium window. The chromatographic analyses (GC) were performed using a Younglin 6100 instrument equipped with a flame ionization detector and a 30 m HP-5 capillary column (0.25 mm diam., 0.33 mm film thickness), using nitrogen (2 mL min⁻¹) as a carrier gas, $T_{\text{injector}} = 270$ °C, $T_{\text{column}} = 60$ °C (3 min) and 60–270 °C (15 °C min⁻¹), $P = 12$ psi. Thin layer chromatography (TLC) was carried out on Schleicher & Schuell F1400/LS 254 plates coated with a 0.2 mm layer of silica gel; detection was done using UV₂₅₄ light. Column chromatography was performed using silica gel 60 of 40–63 mesh. ICP-MS analyses were carried out using a Thermo Elemental VG PQ-ExCell spectrometer.

Synthetic procedures

General procedure for the preparation of PdO-Fe₃O₄ catalyst. To a stirred solution of PdCl₂ (345 mg, 2 mmol) and KCl (2 g, 26 mmol, to increase the palladium solubility) in deionized water (240 mL) was added micro-Fe₃O₄ (8 g, 34 mmol).

After 10 min at room temperature, the mixture was slowly basified with NaOH (1 M) until the pH was around 13. The mixture was stirred for 24 hours at room temperature in air. After that, the catalyst was filtered and washed with deionized water (3 × 10 mL). The solid was dried at 100 °C for 24 h in a standard glassware oven, obtaining the expected catalyst: incorporation of palladium was 2.74% according to XRF.

General procedure for the preparation of DESs. A mixture of a hydrogen-bond donor and a hydrogen-bond acceptor, with the previously specified molar ratio, was added into a round bottom flask under an inert atmosphere. The mixture was stirred for 60 minutes in the T range between 65 and 80 °C, and the corresponding DES is obtained.

General procedure for the preparation of the starting material. 2,2-Dimethylpent-4-ynoic acid (1b), *N*-tosylpent-4-ynamide (1f) and 5-phenylpent-4-ynoic acid (1e) were prepared according to reported procedures.¹³

General procedure of the cycloisomerization reactions. In a 10 mL glass tube, the catalyst PdO–Fe₃O₄ (0.5 mg), the corresponding substrate (0.1 mmol) and the solvent (0.2 mL) were added. Subsequently, the tube was sealed with a septum and heated to the corresponding temperature for the time necessary for each starting reagent. After the reaction was completed, the tube was cooled. Then, the mixture was quenched with water and extracted with AcOEt (3 × 1 mL). The organic phases were dried over MgSO₄, followed by evaporation under reduced pressure to remove the solvent and purified by column chromatography.

Procedure for catalyst recycling. The reaction was performed according to the general procedure. After 10 minutes, the mixture was extracted with ethyl acetate, dissolving all organic compounds, in such a way that water and catalyst remained in the reaction tube. To the remaining mixture, compound 1a was added, carrying out the reaction again under the same reaction conditions.

On the other hand, in order to recycle only the catalyst, we extracted the product with water and AcOEt (3 × 1 mL) and then, upon decanting the solution with the aid of a magnet, the catalyst remained in the reaction tube. Then, fresh water and compound 1a were added to the tube, carrying out the new reaction under standard conditions.

Conclusions

In conclusion, we have demonstrated that palladium(II) oxide impregnated on magnetite is a cheap, selective, versatile and very active catalyst for the cycloisomerization of a variety of alkynoic acids and their derivatives (*i.e.*, alkynyl imides). The little amount of palladium catalyst used was one of the lowest palladium catalyst loadings ever reported. Moreover, the reactions were found: (i) to be highly regio- and stereoselective, resulting in selective formation of the *exo*-dig products and, for internal alkynes, selective formation of the *Z* configuration product; (ii) to take place under air and in sustainable solvents (water and DES); (iii) to occur in the absence of co-catalysts (no bases, acids or halogen extractors are required); and (iv) to be recycled in four consecutive runs without loss of activity or selectivity. Thus, and all-in-all, we have presented a highly efficient and sustainable methodology (that takes place under standard bench conditions) for the synthesis of highly substituted heterocycles (either five-membered lactones or lactams) or acyclic keto-acids or keto-imides, which involves maximum atomic economy and the use of green solvents, which makes the sustainability of the whole process extremely high.

Conflicts of interest

There are no conflicts to declare.

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