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A tailored polymeric cationic tag–anionic Pd(II) complex as a catalyst for the low-leaching Heck–Mizoroki coupling in flow and in biomass-derived GVL⁺

The $[PdCl_4]^{2-}$ palladium complex has been immobilized on a polystyrene-type resin loaded with pincertype imidazolium ionic tag binding sites. The catalytic system (Pd(II)-POLI-TAG) has proved to be highly active in the definition of an efficient protocol for the Heck–Mizoroki coupling reaction under batch and flow conditions. Importantly, it is shown to be highly robust in combination with a safe non-toxic reaction medium, *i.e.* biomass-derived GVL, since it could be reused for multiple runs without significantly losing its activity.

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Introduction

In the last 50 years, palladium-catalyzed cross-coupling reactions have played a fundamental role in shaping chemical synthesis and innovative synthetic strategies in organic chemistry, be it for small or highly complex target systems.^{1,2}

The Pd-catalyzed olefination of alkyl halides (*i.e.* the Heck-Mizoroki reaction) is a widely used synthetic tool empowering the structural motifs often found in, for example, pharmaceuticals, agrochemicals, fine chemicals, and organic semiconductor materials with rapid and convenient access, along with excellent yields.^{3–5}

Motivated mainly by their easy separation and recovery, recycling and reuse, and amenability to continuous processing, possibly leading to waste minimized protocols, several palladium-based heterogeneous catalysts have been proposed for the environmentally friendly Heck–Mizoroki couplings, including palladium on activated carbon, oxides, polymers and zeolites.⁶

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Possible metal leaching from the surface is one of the major drawbacks in heterogeneous Heck-Mizoroki catalysis, since it would make the above arguments invalid. It would also implicate a time-consuming and costly product cleaning step, especially in the case of, for example, the synthesis of active pharmaceutical intermediates, in which metal contamination is a serious issue.⁷ In addition, the metal leached and the change of morphology and metal particle size may modify the heterogeneous catalyst both in its structure and mainly in its catalytic efficiency reproducibility. This is a critical issue that sometimes still makes homogeneous catalysis preferable.7a

Palladium leaching is known to correlate significantly with metal-support interactions as well as reaction parameters.8 For example, Jumde et al.^{8a} reported on the high stabilization of palladium nanoparticles by the pyridyl domain of a 4-vinylpyridine/ethylene glycol dimethacrylate co-polymeric monolith, which demonstrated to be effective as catalyst in the Heck-Mizoroki reaction carried out in a continuous-flow minifluidic device. In the context of the reaction parameters, a marked influence of the reaction medium is often observed.^{8b} It is worth noting that the Heck reaction is still usually performed using hazardous conventional dipolar aprotic solvents,9 such as dimethyl formamide (DMF), dimethylacetamide (DMAc) and N-methyl-2-pyrrolidone (NMP). Besides being highly undesirable from the safety and environmental points of view, conventional dipolar aprotic solvents strongly bind to palladium species, thereby not only facilitating their dissolution from the support with a consequent high reactivity but also largely leaching into the products.¹⁰

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[†]Electronic supplementary information (ESI) available: Experimental section and representative E-factor calculation, full characterization of compounds and copies of the ¹H and ¹³C NMR spectra. See DOI: 10.1039/c8gc03228a [‡]Both authors contributed equally to this work.

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 γ -Valerolactone (GVL), a safe, non-toxic chemical from renewable lignocellulosic biomass, has been proved by us to replace dipolar aprotic solvents in metal-catalyzed cross-coupling reactions.¹¹ Our group also observed that when combining the use of GVL with heterogeneous metal catalysts, this medium tends to minimize metal leaching.

In this context, we also demonstrated that by operating in a continuous flow regime, additional advantages in terms of catalyst lifetime and, ultimately, waste minimization are attained.^{6,11,12}

In this contribution, we report our results on the definition of a tailor-made polymeric ionic tag as a support for palladium(II) featuring high durability and minimal leaching and with the goal of defining a waste-minimized, efficient flow protocol for a clean Heck reaction.

We have developed our protocol by combining the use of GVL as the reaction medium with flow technology exploiting the features of a specifically designed heterogeneous palladium catalyst, consisting of a POLymeric Ionic TAG (POLI-TAG) working as a support for the formation of the palladium(π) complex (Pd(π)-POLI-TAG).

More specifically, we planned the preparation of a novel immobilized anionic palladium complex (1) based on a pincertype imidazolium salt supported on a polystyrene-type structure (Fig. 1), *i.e.* on organic ionic tags. Though anionic species are frequently proposed to participate in cross-coupling catalysis,¹³ the direct use of anionic palladium complexes remains scarce.¹⁴ In particular, to the best of our knowledge, there are no previous reports about the use of supported anionic palladium complexes which do not undergo the formation of an N-heterocyclic carbene (NHC)-metal bond, eventually leading to a notable decrease in catalyst efficiency.¹⁵

The catalyst was designed bearing in mind that ionic moieties are able to selectively scavenge metal catalytic species, allowing for their recycling.^{14c,16,17} Additionally, pincer-type coordination to palladium species is expected to offer the advantage of enhanced complex stability.¹⁸ For the support, we focused on a styrene/vinylbenzylchloride/1,4-bis(4-vinylphenoxy)benzene copolymer (**SP**) since our previous studies¹⁷ have proved that this polymer exhibits high thermal and mechanical stability, high compatibility with a range of safer (green) polar reaction media and enables chloride substitution under relatively mild conditions.

Our results demonstrate that catalyst **1** can be reused for multiple runs without significant Pd leaching from the surface into the reaction solution under the applied reaction conditions.



Fig. 1 Architecture of imidazolium-based heterogeneous palladium catalyst 1 (Pd(μ)-POLI-TAG).

Results and discussion

Catalyst synthesis and characterization

The preparation of palladium(II)-based catalyst 1 begins with the reaction of polystyrene-type resin SP-Cl¹⁸ (2) (styrene/vinylbenzylchloride/1,4-bis(4-vinylphenoxy)benzene = 0.83/0.15/0.2) with 3,3-bis(1*H*-imidazol-1-yl)propan-1-ol (3) in the presence of NaH (Scheme 1) to afford the intermediate 4, exhibiting a loading of bis-imidazole units of 0.76 mmol g⁻¹. 3,3-Bis(1*H*imidazol-1-yl)propan-1-ol (2) is, in turn, synthesized *via* hydroamination of methyl propiolate by 1*H*-imidazole under solvent-free conditions, and subsequent reduction with LiAlH₄ of the resulting methyl-3,3-bis(1*H*-imidazol-1-yl)propanoate (see the ESI† for the experimental details). In the subsequent step, the derivative 4 is subjected to a quaternization reaction by employing iodomethane to provide the polymer-supported imidazolium salt 5, with a bis-imidazolium moiety loading of 0.51 mmol g⁻¹ (Scheme 1).

Fig. S1–S3 (ESI[†]) report the solid-state ¹³C cross-polarization magic angle spinning (CP-MAS) NMR spectra of materials 2 and 5, respectively. CP-MAS spectra at different spinning frequencies (8 kHz and 10 kHz) were employed to identify the spinning sidebands (ESI[†]). NMR experiments using the "total suppression of spinning side bands" (TOSS) sequence were performed as well (Fig. S3a[†]). A comparison of the spectra before and after quaternization allows evidencing a significant decrease of the signal centered at around 45 ppm that can be reasonably assigned to the carbon of benzyl chloride. This observation represents an indication of the functionalization of the polymeric support. An in-depth NMR investigation employing the non-quaternary and non-methyl suppression (NQS) sequence was also performed (Fig. S3b[†]). It is known that NQS experiments allow the removal of mainly the contributions relative to the secondary and tertiary carbons while the signals corresponding to the primary



Scheme 1 Synthetic route to heterogeneous catalytic system 1.

carbons are only slightly decreased. Sample 5 displays a contribution at around 36 ppm corresponding to the methyl functionality, indicating a good performance of the quaternization reaction.

To pursue the formation of the supported anionic palladium complex (1), derivative 5 was stirred with an aqueous solution of $[PdCl_4]^{2-}$, generated *in situ* from $PdCl_2$ and NaCl(Scheme 1). Microwave plasma-atomic emission spectrometry (MP-AES) revealed a loading of Pd(n) of 3 wt%.

Catalytic activity

The efficiency of the new immobilized anionic palladium complex (1) has been first tested in the Heck-Mizoroki reaction under conventional batch conditions. Thus, the representative reaction between iodobenzene (**6a**) and a slight excess (20%) of methylacrylate (7a) (Table 1) was carried out in GVL (0.8 M with respect to **6a**) with polystyrene-supported triethylamine (PS-TEA) as a heterogeneous base (Table 1, entry 1). PS-TEA has already proved to be effective in providing a more efficient isolation of the product compared to the homogeneous counterpart.⁶

Under the selected conditions, a quantitative conversion into the desired product **8aa** was obtained. Notably, MP-AES analyses revealed negligible palladium leaching (0.37 ppm).

For comparison purposes, the use of a homogeneous triethylamine (TEA) base led to metal leaching about four times higher (Table 1, entry 2), which is attributable to the higher ability of TEA to coordinate active Pd species from the heterogeneous catalyst, thereby increasing the amount of the leached metal in the solvent.⁶

Next, we analyzed the behavior of our system in different media, both in terms of the conversion to product **8aa** and the palladium leaching issue. By employing conventional dipolar aprotic solvents (*i.e.* DMAc, DMF, and NMP), the model substrates **6a** and **7a** showed high reactivity, but a somewhat

 Table 1
 The Heck reaction^a of iodobenzene 6a and methyl acrylate 7a

 in different reaction media, and the corresponding data for palladium leaching

	6a +		1 (0.1 mol%) PS-TEA, medium 130°C, 2 h	Baa
Entry	Medium		C^{b} (%)	Pd-Leaching ^c (ppm)
1	GVL		>99 (91)	0.37
2^d	GVL		>99	1.44
3	DMAc		>99	2.01
4	DMF		>99	1.25
5	NMP		>99	1.60
6	$DMF/H_2O(4:1)$		>99	3.18
7	CH ₃ CN/H ₂ O az		>99	1.20

^{*a*} Reaction conditions: **6a** (1 mmol), **7a** (1.2 mmol), base (1.5 mmol), solvent (1.25 mL), 130 °C, 2 h. ^{*b*} Conversion determined by GLC analyses, yields of isolated products are given in parenthesis. ^{*c*} Determined by MP-AES analyses. ^{*d*} Homogeneous triethylamine base was used.

greater amount of leached palladium species was measured (Table 1, entries 3–5). A similar behavior was observed for a DMF-water mixture and an acetonitrile azeotrope (Table 1, entries 6 and 7).

It is worth noting that a low residual palladium content has, however, been measured in all cases, and, with reference to the use of GVL in combination with PS-TEA, it is well below the strict specification limits for the residual metal in, for example, pharmaceutical targets⁷ (*vide supra*). This indicates good catalyst stability under different conditions (*i.e.* a strong metal-supported IL interaction) and easy purification of the product. Furthermore, these findings suggest that the Heck cross-coupling catalyzed by **1** is either authentically heterogeneous or may proceed through a so-called "release and catch" mechanism.¹⁹

We also investigated the recovery and reuse of catalyst **1** under the optimized conditions.

To recover the catalyst, it was indeed necessary to also recover and regenerate the base, since the catalyst cannot be separated from the solid base after filtration. Thus, the solid mixture of catalyst **1** and PS-TEA was first quantitatively recovered using a classical filtration technique, then washed with a solution of TEA in GVL (1.5 equiv. with respect to the supported base) to displace the hydroiodic acid reaction byproduct from PS-TEA. The solid mixture was then washed with some GVL to remove residual TEA and efficiently reused in a subsequent run (Fig. 2). Notably, the GVL used in the regeneration/wash steps could be nearly quantitatively recovered by distillation (97%).

The catalyst reuse was repeated for four representative reaction runs, and it was found that conversion to **8aa** was substantially retained, with the system **1**-PS-TEA undergoing regeneration treatment in between runs (Fig. 2).

The good durability of the catalytic system was also confirmed by MP-AES analyses, which constantly revealed a negligible palladium leaching for each reaction run, with an average value of about 0.3 ppm (Fig. 2). This excellent result corresponds to a catalyst turnover number (TON) of 4870 and a turnover frequency (TOF) of 487 h^{-1} .

Reaction scope

To broaden the reaction scope, several (hetero)aryl iodides 6 were reacted with acrylates 7 (Scheme 2) and styrenes 9



Fig. 2 Reusability of catalyst 1 for the Heck–Mizoroki reaction to 8aa.



(Scheme 3) using the optimal conditions, and good to excellent yields (76–93%) were obtained in a short time (2 h). In the case of the reaction between 2-iodothiophene (**6e**) and alkyl acrylate **7a** or **7b** (Scheme 2), traces of the homocoupling byproduct 2,2'-bithiophene **12** was obtained (below 4%, Table S1, ESI†).

When styrenes **9** were employed, a small amount of *gem*substituted regioisomers **11** was detected in all cases. By reacting 2-iodothiophene, the homocoupling by-product **12** was additionally formed, but stilbenes **10ea** and **10eb** were easily obtained in a pure form by the precipitation work up (Scheme 3 and Table S1[†]).

To realize a truly waste-minimized protocol, we also focused our attention on the work-up procedure. Notably, after the removal of the catalyst 1-PS-TEA system by filtration, the

1 (0.1 mol%) PS-TEA, GVL Ar 130°C. 2 h 10 11 12 6 9 R MeO R= H (10ca): 89% R= H (10ba): 86% R= H (10aa): 85% R= CI (10bb): 82% R= CI (10cb): 90% R= CI (10ab): 87% R= H (10ea): 76%^t R= H (10da): 93% R= CI (10eb): 80%b R= Cl (10db): 89%

Scheme 3 Synthesis of stilbenes 10.^a Reaction conditions: 6 (1 mmol), 9 (1.2 mmol), base (1.5 mmol), GVL (1.25 mL), 130 °C, 2 h. ^bAfter column chromatography.

pure product could be conveniently isolated either by direct precipitation from the reaction mixture with a minimal amount of water, due to the high solubility in this medium of GVL or by extraction with *n*-heptane, depending on the formation of solid or oily products, respectively.

On the bases of the optimized results obtained under classical batch conditions, we have set a flow protocol by charging a stainless-steel column reactor of an appropriate length with a mixture of catalyst **1** and the supported base PS-TEA dispersed in glass beads ($\emptyset = 1 \text{ mm}$), while a pre-mixed solution of **6a** and **7a** was charged in a glass column, acting as the reservoir. The equipment was then connected, by using the appropriate valves, to a pump and installed into a thermostatted box. The temperature was set at 130 °C and, subsequently, the reaction mixture was continuously pumped (flow rate: 1.0 mL min⁻¹) through the base–catalyst column until complete conversion of the reactants into product **8aa** was achieved (2 h, Table 2, entry 1).

Next, a solution of TEA (1.5 equiv. in 2 mL of GVL) was cyclically pumped through the base–catalyst column (flow rate: 1 mL min⁻¹; 30 min) to regenerate PS-TEA. The column was then cyclically washed with GVL (2.5×2 mL) and pumped through the base–catalyst column to remove residual TEA. After this treatment, a second batch of **6a** and **7a** was charged in the reservoir, and a quantitative conversion to product **8aa** was achieved again after 2 h (Table 2, entry 2).

By employing the same flow reactor, different substrates were quantitatively reacted under the above conditions. More specifically, our optimized flow reaction conditions proved to be effective for representative **6d**, **9a** and **6e**, **9b** substrates (Table 2, entries 3 and 4, and 5 and 6, respectively).

Interestingly, the reaction between **6d** and **9a** was completely selective towards the target product **10da** compared to the one under classical batch conditions, for which **10da** : **11da** = 94 : 6 was obtained (Table S1[†]).

Table 2 Catalyst reusability in a flow reactor for the representative

Heck–Mizoroki couplings^a



 a Reaction conditions: Iodoarene (1 mmol), styrene 9 or acrylate 7 (1.2 mmol), PS-TEA (3.2 mmol g⁻¹), GVL (1.2 mL), 130 °C, 2 h. b Conversion determined by GLC analyses, yields of isolated products are given in parenthesis. c Determined by MP-AES analysis.

 Alk

 A

To further evaluate the durability of the catalytic system **1** we have quantified the amount of palladium species leached in the mixture at the end of each reaction cycle, and it is worth noting that such an amount was consistently negligible, with an average value of 0.05 ppm.

These results correspond to TON and TOF values higher than those for the batch mode, *i.e.* 5940 and 495 h^{-1} , respectively.

The GVL used in the reaction was distilled off and nearly quantitatively recovered with a purity comparable to the starting solvent (¹H-NMR analysis).

To evaluate our results in terms of sustainability, we calculated the associated environmental factor $(E-factor)^{20}$ values of both batch and flow protocols in GVL as the medium (see the ESI† and Table 2).

While for batch conditions, E-factor values are in the range of 21–75 (or 14.5–63.7, when considering GVL recovery, see above), under flow conditions, these values resulted in a marked reduction, and E-factors in the range of 2.4–5 are achieved. This is an important feature proving the effectiveness of the flow approach since it allowed us to maintain the amount of waste produced low. In addition, the stability of the leaching phenomenon, which is the main feature of our Pd(n)-POLI-TAG solid catalyst, can be most efficiently exploited under flow conditions where the catalyst remains closed in the reactor and can be reused without any manipulation. Low leaching and flow conditions ensure a very high stability and durability of the catalyst that is able to consistently give identical reproducible results in terms of both catalytic efficiency and metal contamination of the products.

Conclusion

The immobilization of an anionic palladium complex on a polystyrene-type resin loaded with pincer-type imidazolium salt binding sites provided a highly stable catalyst (Pd(II)-POLI-TAG), and no evidence of the formation of NHC was observed. A low amount (0.1 mol%) of the catalyst was used in the widely representative Heck–Mizoroki reaction in GVL as a safe and recoverable reaction medium. It demonstrated a high activity over consecutive runs with a negligible release of the metal. Finally, the durability and reusability of the catalyst as well as waste production during the process have been considerably improved by means of flow technology, as also confirmed by the very low E-factor values achieved.

Conflicts of interest

There are no conflicts of interest to declare.

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Notes and references

- (a) N. Miyaura, K. Yamada and A. Suzuki, *Tetrahedron Lett.*, 1979, 20, 3437-3440; (b) D. Milstein and J. K. Stille, *J. Am. Chem. Soc.*, 1978, 100, 3636-3638; (c) A. O. King, N. Okukado and E. Negishi, *J. Chem. Soc., Chem. Commun.*, 1977, 683-684; (d) K. Sonogashira, Y. Tohda and N. Hagihara, *Tetrahedron Lett.*, 1975, 16, 4467-4470; (e) K. Tamao, K. Sumitani and M. Kumada, *J. Am. Chem. Soc.*, 1972, 94, 4374-4376; (f) R. F. Heck, *J. Am. Chem. Soc.*, 1968, 90, 5518-5526.
- 2 (a) D. J. Burke and D. J. Lipomi, *Energy Environ. Sci.*, 2013,
 6, 2053–2066; (b) C. Toborg and M. Beller, *Adv. Synth. Catal.*, 2009, 351, 3027–3043; (c) *Handbook of Organopalladium Chemistry for Organic Synthesis*, ed. E. Negishi, John Wiley & Sons, New York, 2002, vol. 1.
- 3 (a) C. B. Ziegler and R. F. Heck, J. Org. Chem., 1978, 43, 2941-2946; (b) H. A. Dieck and R. F. Heck, J. Am. Chem. Soc., 1974, 96, 1133-1136; (c) R. F. Heck and J. P. Nolley, J. Org. Chem., 1972, 37, 2320-2322; (d) R. F. Heck, J. Am. Chem. Soc., 1971, 93, 6896-6901; (e) R. F. Heck, J. Am. Chem. Soc., 1969, 91, 6707-6714.
- 4 (*a*) K. Mori, T. Mizoroki and A. Ozaki, *Bull. Chem. Soc. Jpn.*, 1973, **46**, 1505–1508; (*b*) T. Mizoroki, K. Mori and A. Ozaki, *Bull. Chem. Soc. Jpn.*, 1971, **44**, 581.
- 5 (a) S. Jagtap, *Catalysts*, 2017, 7, 267; (b) *The Mizoroki-Heck Reaction*, ed. M. Oestreich, John Wiley & Sons, 2009.
- 6 For representative examples see: (a) A. Zhou, R.-M. Guo, J. Zhou, Y. Dou, Y. Chen and J.-R. Li, ACS Sustainable Chem. 2018, 6, 2103-2111; (b) P. Veerakumar, Eng., P. Thanasekaran, K.-L. Lu, S.-B. Liu and S. Rajagopal, ACS Sustainable Chem. 2017, Eng., 5, 6357-6376; (c) R. S. B. Gonçalves, A. B. V. de Oliveira, H. C. Sindra, B. S. Archanjo, M. E. Mendoza, L. S. A. Carneiro, C. D. Buarque and P. M. Esteves, ChemCatChem, 2016, 8, 743-750; (d) C. Petrucci, M. Cappelletti, O. Piermatti, M. Nocchetti, M. Pica, F. Pizzo and L. Vaccaro, J. Mol. Catal. A: Chem., 2015, 401, 27-34; (e) C. Petrucci, G. Strappaveccia, F. Giacalone, M. Gruttadauria, F. Pizzo and L. Vaccaro, ACS Sustainable Chem. Eng., 2014, 2, 2813-2819.
- 7 (a) S. Hübner, J. G. de Vries and V. Farina, Adv. Synth. Catal., 2016, 358, 3–25; (b) C. E. Garrett, Adv. Synth. Catal., 2004, 346, 889–900; (c) Note for Guidance on Specification Limits for Residues of Metal Catalysts, The European Agency for the Evaluation of Medicinal Products, Evaluation of Medicines for Human Use; London, 17 December 2002; http://www.emea.eu.int.

- 8 (a) R. P. Jumde, M. Marelli, N. Scotti, A. Mandoli, R. Psaro and C. Evangelisti, *J. Mol. Catal. A: Chem.*, 2016, 414, 55– 61; (b) C. Sievers, Y. Noda, L. Qi, E. M. Albuquerque, R. M. Rioux and S. L. Scott, *ACS Catal.*, 2016, 6, 8286–8307.
- 9 (a) S. B. Park and A. Howard, Org. Lett., 2003, 5, 3209–3212;
 (b) A. Spencer, J. Organomet. Chem., 1983, 258, 101–108.
- 10 (a) Regulation 1907/2006/EC of 18 December 2006 Concerning the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH), Establishing а European Chemicals Agency, Amending Directive 1999/45/ EC and Repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/ EEC, 93/67/EEC, 93/105/EC and 2000/21/EC, [2006] OJ L396/1('REACH'). (b) J. Kuwabara, T. Yasuda, S. J. Choi, W. Lu, K. Yamazaki, S. Kagaya, L. Han and T. Kanbara, Adv. Funct. Mater., 2014, 24, 3226-3233; (c) M. P. Nikiforov, B. Lai, W. Chen, S. Chen, R. D. Schaller, J. Strzalka, J. Maserb and S. B. Darling, Energy Environ. Sci., 2013, 6, 1513-1520; (d) P. A. Troshin, D. K. Susarova, Y. L. Moskvin, I. E. Kuznetsov, S. A. Ponomarenko, E. N. Myshkovskaya, K. A. Zakharcheva, A. A. Balakai, S. D. Babenko and V. F. Razumov, Adv. Funct. Mater., 2010, 20, 4351-4357.
- (a) F. Ferlin, L. Luciani, S. Santoro, A. Marrocchi, D. Lanari, A. Bechtoldt, L. Ackermann and L. Vaccaro, *Green Chem.*, 2018, 20, 2888–2893; (b) F. Ferlin, S. Santoro, L. Ackermann and L. Vaccaro, *Green Chem.*, 2017, 19, 2510–2514; (c) S. Santoro, F. Ferlin, L. Luciani, L. Ackermann and L. Vaccaro, *Green Chem.*, 2017, 19, 1601–1612; (d) G. Strappaveccia, E. Ismalaj, C. Petrucci, D. Lanari, A. Marrocchi, M. Drees, A. Facchetti and L. Vaccaro, *Green Chem.*, 2015, 17, 365–372; (e) G. Strappaveccia, L. Luciani, E. Bartollini, A. Marrocchi, F. Pizzo and L. Vaccaro, *Green Chem.*, 2015, 17, 1071–1076.
- 12 L. Vaccaro, D. Lanari, A. Marrocchi and G. Strappaveccia, *Green Chem.*, 2014, **16**, 3680–3704.
- 13 (a) F. Proutiere and F. Schoenebeck, Angew. Chem., Int. Ed., 2011, 50, 8192–8195; (b) B. P. Carrow and J. F. Hartwig, J. Am. Chem. Soc., 2010, 132, 79–81; (c) L. J. Goossen, D. Koley, H. L. Hermann and W. Thiel, J. Am. Chem. Soc., 2005, 127, 11102–11114; (d) A. H. M. De Vries, F. J. Parlevliet, L. Schmieder-van de Vondervoort, J. H. M. Mommers, H. J. W. Henderickx, M. A. M. Walet and J. G. De Vries, Adv. Synth. Catal., 2002, 344, 996–1002; (e) C. Amatore and A. Jutand, Acc. Chem. Res., 2000, 33, 314–321.
- 14 For recent representative examples see: (a) F. Schroeter, J. Soellner and T. Strassner, ACS Catal., 2017, 7, 3004–3009;
 (b) E. Silarska, A. M. Trzeciak, J. Pernak and A. Skrzypczak,

J. Mol. Catal. A: Chem., 2017, **426**, 458–464; (c) L. A. Bivona, F. Giacalone, E. Carbonell, M. Gruttadauria and C. Aprile, *ChemCatChem*, 2016, **8**, 1685–1691; (d) H. Song, N. Yan, Z. Fei, K. J. Kilpin, R. Scopelliti, X. Li and P. J. Dyson, *Catal. Today*, 2012, **183**, 172–177; (e) W. Zawartka, A. Gniewek, A. M. Trzeciak, J. J. Ziółkowski and J. J. Pernak, J. Mol. *Catal. A: Chem.*, 2009, **304**, 8–15.

- 15 (a) M.-A. Neouze, J. Mater. Chem., 2010, 20, 9593–9607;
 (b) P. Migowski and J. Dupont, Chem. Eur. J., 2007, 13, 32–39;
 (c) W. Zawartka, A. M. Trzeciak, J. J. Ziółkowski, T. Lis, Z. Ciunik and J. Pernak, Adv. Synth. Catal., 2006, 348, 1689–1698;
 (d) A. J. Carmichael, M. J. Earle, J. D. Holbrey, P. B. McCormac and K. R. Seddon, Org. Lett., 1999, 1, 997–1000.
- 16 (a) M. Gruttadauria, L. F. Liotta, A. M. P. Salvo, F. Giacalone, V. La Parola, C. Aprile and R. Noto, Adv. Synth. Catal., 2011, 353, 2119–2130; (b) M. I. Burguete, E. Garcìa-Verdugo, I. Garcia-Villar, F. Gelat, P. Licence, S. V. Luis and V. Sans, J. Catal., 2010, 269, 150; (c) B. Karimi, D. Elhamifar, J. H. Clark and A. J. Hunt, Chem. - Eur. J., 2010, 16, 8047-8053; (d) M.-J. Jin, A. Taher, H.-J. Kang, M. Choi and R. Ryoo, Green Chem., 2009, 11, 309-313; (e) H. Yang, X. Han, G. Li and Y. Wang, Green Chem., 2009, 11, 1184-1193; (f) J. Y. Shin, B. S. Lee, Y. Jung, S. J. Kim and S.-g. Lee, Chem. Commun., 2007, 5238-5240; (g) M. J. Park and S.-g. Lee, Bull. Korean Chem. Soc., 2007, 28, 1925-1926; (h) J.-W. Kim, J.-H. Kim, D.-H. Lee and Y.-S. Lee, Tetrahedron Lett., 2006, 47, 4745-4748; (i) J.-H. Kim, J.-W. Kim, M. Shokouhimehr and Y.-S. Lee, J. Org. Chem., 2005, 70, 6714-6720.
- 17 (a) V. Trombettoni, D. Sciosci, M. P. Bracciale, F. Campana, M. L. Santarelli, A. Marrocchi and L. Vaccaro, *Green Chem.*, 2018, 20, 3222–3231; (b) M. Tassi, E. Bartollini, P. Adriaensens, L. Bianchi, B. Barkakaty, R. Carleer, J. Chen, D. K. Hensley, A. Marrocchi and L. Vaccaro, *RSC Adv.*, 2015, 5, 107200–107208; (c) A. Marrocchi, P. Adriaensens, E. Bartollini, B. Barkakati, R. Carleer, J. Chen, D. K. Hensley, C. Petrucci, M. Tassi and L. Vaccaro, *Eur. Polym. J.*, 2015, 73, 391–401.
- 18 *The Chemistry of Pincer Compounds*, ed. D. Morales-Morales and C. M. Jensen, Elsevier Science B.V., 2007.
- (a) V. Kozell, T. Giannoni, M. Nocchetti, R. Vivani,
 O. Piermatti and L. Vaccaro, *Catalysts*, 2017, 7, 186;
 (b) C. Pavia, F. Giacalone, L. A. Bivona, A. M. P. Salvo,
 C. Petrucci, G. Strappaveccia, L. Vaccaro, C. Aprile and
 M. Gruttadauria, *J. Mol. Catal. A: Chem.*, 2014, 387, 57–62;
 (c) M. Gruttadauria, F. Giacalone and R. Noto, *Green Chem.*, 2013, 15, 2608–2618.
- 20 R. A. Sheldon, Chem. Commun., 2008, 3352-3365.