Iminopyridyl-palladium dendritic catalyst precursors: evaluation in Heck reactions

Gregory S. Smith, Selwyn F. Mapolie*

Department of Chemistry, University of the Western Cape, Private Bag X17, Bellville 7535, South Africa

Abstract

Poly(propyleneimine)-iminopyridyl-palladium dendrimers, bearing palladium moieties on the periphery, were found to be effective catalyst precursors for Heck coupling. The dendritic complexes achieved high conversions in the reaction of iodobenzene with methyl acrylate, styrene and 1-octene. Reactions with electron-deficient olefins yield mainly β-arylated products, whilst electron-rich olefins, yield a mixture of arylated products (β, α), *cis/trans* isomers and β,β-disubstituted compounds. Generally, the metallodendrimer leads to higher conversions and the reactions proceed at a faster reaction rate, when compared to reactions using an analogous mononuclear palladium complex or the palladium salt, $PdCl_2$.
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1. Introduction

The Heck reaction is widely used in organic transformations in the synthesis of various substituted olefins and dienes [1–3], and entails the cross-coupling reaction of electron-rich organohalides and pseudohalides with a wide range of olefins. This reaction has been limited to laboratory research and there are few examples of industrial application [4].

Since the discovery of the Heck reaction, there have been increasing reports of synthetic applications, improvements of traditional Heck conditions, studies of regio- and stereo-selectivity and new discoveries on mechanistic features [5,6]. Traditionally, homogeneous catalytic systems have been used and are highly effective, although heterogeneous catalysts are preferred [7]. Techniques demonstrating the immobilisation of various complexes are well documented [8–10]. For example, Teranishi and co-workers have immobilised palladium on phosphinated polystyrene [11], for various carbon–carbon bond-forming reactions. Hallberg and co-workers [12] and Zhang et al. [13] also reported polymer-supported catalysts in Heck arylation reactions. Clark et al. [14] prepared a novel palladium catalysts supported on chemically modified mesoporous silica gel, for use in the coupling of aryl iodides with olefins.

Dendritic-metal complexes are becoming increasingly popular in various catalytic processes, as they offer the advantages of acting as both heterogeneous and homogeneous catalyst precursors. These materials would ideally be recoverable and recyclable, yet still maintain a high activity. The use of dendritic supports has also found particular application in the Heck reaction [15]. The best example is Reetz's dendritic phosphine [15,16], DAB-*dendr*-[N(CH$_2$PPh$_2$)$_2$]$_{16}$, bearing P-centres on the periphery, co-ordinated to palladium catalysts. Alper et al. [17] affixed polyamidoamidodiphosphonated dendrimers on the surface of silica and complexed these to form a palladium–dimethyl TMEDA complex. These catalysts are effective in coupling aryl bromides with butyl acrylate and styrene, and could be reused with a moderate loss in activity. Screttas and co-workers recently employed an iminophosphine dendrimeric ligand to perform various Heck coupling reactions [18]. Recent reports involving Pd(II)/diazobutadiene systems [19] as active catalysts for the Heck arylation of olefins, prompted us to investigate the application of the first-generation metallodendrimer **1**, DAB-G1(impyr-PdCl$_2$)$_4$, as a potential Heck cross-coupling catalyst precursor. The results from our preliminary investigations are reported in this paper.

* Corresponding author. Tel.: +27-21-9593049; fax: +27-21-9593055.
E-mail address: smapolie@uwc.ac.za (S.F. Mapolie).

2. Experimental

2.1. Materials

All solvents were dried over the appropriate drying agents and distilled prior to use. $PdCl_2$ and triethylamine were obtained from Merck. Iodobenzene was obtained from Hopkin and Williams Ltd., and distilled prior to use. Methyl acrylate was purchased from BDH Chemicals. Styrene and 1-octene were purchased from Sigma–Aldrich. The catalyst precursor **1** was prepared according to the method recently report by our group [20]. The second-generation metallodendrimer **3** was prepared in an analogous manner and is described below. ^1H NMR (200 MHz) and ^{13}C NMR (50 MHz) spectra were recorded on a Varian XR200 spectrometer. GC–MS analyses were performed on a Finnigan MAT GCQ GC/mass spectrometer, equipped with a HP5-MS column.

2.2. Synthesis of the second-generation dendritic ligand

The synthesis of the second-generation dendritic ligand required to prepare the metallodendrimer **3**, was similar to that of the first-generation tetrafunctional iminopyridyl ligand reported in the literature [20] and is briefly described here.

A round-bottomed flask was charged with dry toluene (60 ml). Anhydrous $MgSO_4$ ($\sim$5 g) was transferred to the flask. 2-Pyridinecarboxaldehyde (1.92 g, 17.9 mmol) was syringed into the round-bottomed flask and the mixture stirred at room temperature. A sample of the DAB-*dendr*-$(NH_2)_8$ (1.75 g, 2.26 mmol) was dissolved in 5 ml of dry toluene. This toluene solution was added dropwise to the stirring mixture of the aldehyde and $MgSO_4$. The reaction was allowed to proceed at room temperature for 2 days. The mixture was filtered by gravity and the solvent removed from the filtrate by rotary evaporation with gentle heating ($\sim$40 °C). The residual oil was extracted with hot MeOH and the solvent removed from the extract. The remaining oil obtained from the extract was dissolved in CH_2Cl_2 (20 ml) and washed copiously with water (7 × 50 ml). The organic layer was collected, dried over anhydrous $MgSO_4$ and filtered by gravity. Removal of the solvent by rotary evaporation yielded the desired product as an orange oil (1.06 g). Yield = 32%. Anal. Found: C, 70.17%; H, 8.49%; N, 20.18%. Calc. for $C_{88}H_{120}N_{22}\cdot(1/2)CH_2Cl_2$: C, 69.54%; H, 7.97%; N, 20.16%. ^1H NMR (200 MHz, CDCl$_3$): δ 1.33 (br m, 4H); 1.53 (br m, 8H); 1.80 (qn, 16H); 2.35–2.49 (overlapping m, 36H); 3.63 (t, 16H); 7.22 (t, 8H); 7.62 (t, 8H); 7.90 (d, 8H); 8.32 (s, 8H); 8.56 (d, 8H). ^{13}C NMR (50 MHz, CDCl$_3$): δ 24.6, 28.2, 51.7, 52.3, 54.2, 59.5, 121.1, 124.5, 136.4, 149.3, 154.6, 161.8; IR (neat oil, NaCl plates): 1650, 1589, 1568 cm^{-1} (νC=N).

2.3. Synthesis of second-generation metallodendrimer 3

A Schlenk tube was evacuated and then filled with nitrogen. $PdCl_2(COD)$ (0.170 g, 0.595 mmol) was transferred

to the Schlenk tube. This was dissolved in dry CH_2Cl_2 (15 ml). The iminopyridyl ligand (0.105 g, 0.071 mmol) was dissolved separately in dry CH_2Cl_2 (5 ml). This solution was added to the palladium precursor solution in the Schlenk tube and the mixture stirred at room temperature under nitrogen. After a few minutes, an orange precipitate was formed. The reaction was allowed to proceed for 2 days, and the solid was collected on a Hirsch funnel. The solid was washed with CH_2Cl_2 and dried under vacuum, yielding an amorphous, light orange solid.

Yield = 0.190 g (93%). Melting point: 200 °C (on-set of dec., no melting before 300 °C);

Anal. Found: C, 34.45%; H, 4.38%; N, 9.03%. Calc. for $C_{88}H_{120}N_{22}Pd_8Cl_{16}\cdot4CH_2Cl_2$: C, 34.07%; H, 3.98%; N, 9.50%. ^1H NMR (DMSO-d$_6$): 2.29–2.78 (br signals, core), 3.78 (br t, 8H, –CH_2–N=), 7.85, 8.20, 8.35, 8.90 (br, pyridine), 8.76 (br s, –N=CH–); I.R. (Nujol between NaCl plates): 1599 cm^{-1} (νC=N).

2.4. General procedure for Heck reaction

Iodobenzene (30 mmol), triethylamine (30 mmol) and 30 mmol of an olefin substrate (methyl acrylate, styrene or 1-octene) were mixed in a two-necked round-bottomed flask fitted with a condenser. The mixture was dissolved in 30 ml of dry acetonitrile. The palladium catalyst (0.282 mmol) was added and the mixture heated at 82 °C in an oil bath. Samples of $\sim$0.25 ml were withdrawn periodically by syringe, diluted in dichloromethane and analysed by GC–MS. The conversions were calculated based on *n*-hexadecane as internal standard.

3. Results and discussion

Our studies focused largely on the dendritic palladium complex **1** (Fig. 1), as the palladium source, although some reactions with the second-generation dendrimer were also carried out. All reactions were performed in refluxing acetonitrile. Iodobenzene was chosen as the organohalide substrate, as this is the most reactive of the haloarene family. When aryl iodides are used, the addition of phosphine is not required, which, in fact, inhibits the reaction. Cross-coupling
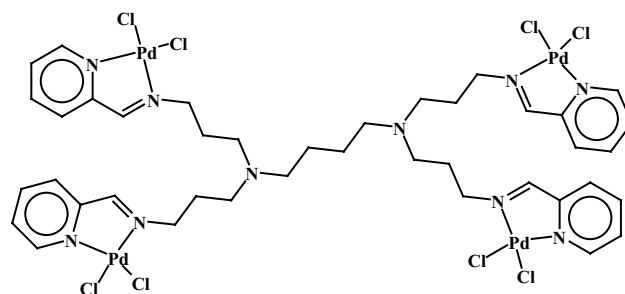

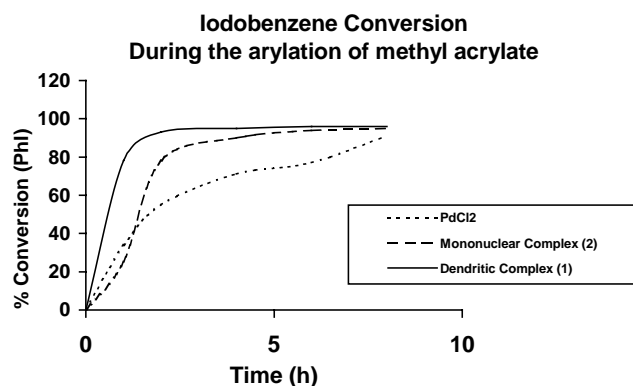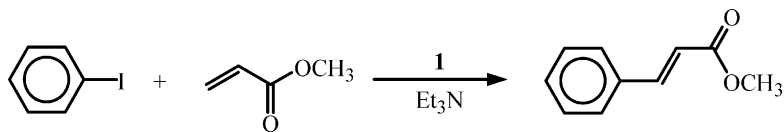Fig. 1. First-generation pyridylimine palladium dendrimer (**1**).

Fig. 2. Conversion as a function of time for the arylation of methyl acrylate with iodobenzene.

Fig. 3. Dichloro-*N-n*-propyl-2-pyridylmethyliminepalladium(II) (**2**).

reactions were attempted with a range of olefins. These include methyl acrylate, styrene and 1-octene. Triethylamine was used to remove hydrogen iodide formed as a by-product during the reaction. All the reactions start after a short induction period of ∼5 min for the mononuclear complexes and ∼10 min for the dendritic complex, in which the initial orange suspension becomes a dark red solution. No attempts were made to recover the catalyst at the end of the reaction.

3.1. Catalytic reactions with methyl acrylate

Complex **1** effectively catalyses the arylation of methyl acrylate (Eq. (1)) in refluxing acetonitrile (82 °C) over 8 h. Using palladium loadings of 0.288 mmol Pd, the aryl iodide was converted to the desired product, methyl 3-phenylprop-2-enoate (methyl cinnamate). The consumption of iodobenzene was monitored and analysed by GC–MS. The conversion of iodobenzene was calculated based on *n*-hexadecane as internal standard.

During the reaction with PdCl$_2$, partial decomposition to residual palladium metal, as palladium black formation was observed. This is possibly the reason for the lower activity. Primary particles formed in solution upon reduction have a tendency to agglomerate to form larger metallic particles. Palladium is generally kept in solution as its phosphine complex, rather than precipitating out as the metal. For complex **1** no undesired formation of elemental Pd was observed. The dendrimer therefore acts as a good support and retards the tendency of the metal sites to agglomerate and precipitate from solution.

Pittman and Ng [21] co-ordinated palladium(0) catalysts to polymer matrices and have shown that these resin-bound catalysts have lower levels of metal agglomeration, a phenomenon commonly observed for many homogeneous catalysts.

The known mononuclear complex, dichloro-*N-n*-propyl-2-pyridylmethyl-iminepalladium(II) (**2**) [22] (Fig. 3), also effectively catalyses the reaction of iodobenzene with methyl acrylate, with a 95% conversion of iodobenzene in 8 h. However, it shows a much slower initial rate in comparison with the dendrimer **1**, with only a 25% conversion of iodobenzene after 1 h.

This catalyst also shows high activity as a Heck catalyst, even though small amounts of palladium black were observed after the reaction was stopped. This lends weight to our proposal that complex **1** acts as a better support,

(1)

The dendritic complex **1** shows a 78% conversion after 1 h and eventually leads to a 96% conversion after 8 h (Fig. 2). This reaction leads to the regiospecific formation of the *trans* isomer, methyl cinnamate, as the major product. A minor amount of the β,β-disubstituted product was found, which is normally only observed in considerable yields in certain reactions where the combined use of high temperature and high pressure is required. A control reaction (no ligand) was run, using only PdCl$_2$ at the same palladium concentration as for the dendritic complex. This was found to be an active catalyst with a 91% conversion at 8 h. It, however, shows much lower conversion during the initial stages of the reaction, showing less than 50% conversion after 2 h reaction time. With respect to catalyst activity, the dendritic complex **1** shows a higher conversion and the reaction proceeds at a much faster initial rate compared to the palladium salt.
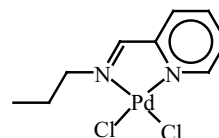
preventing catalyst agglomeration and the precipitation of catalytically inactive palladium metal. The mononuclear complex **2** also shows a slightly higher activity than the palladium salt, PdCl$_2$. This ligand effect is attributed to the σ-donating and low π-accepting abilities of the α-diimine ligand bonded to palladium. The rate of formation of the coupled product using **1** exceeds that of the mononuclear palladium complex **2** and the salt PdCl$_2$. After 8 h, the reactions using the three different catalysts were nearly complete, showing over 95% conversion of iodobenzene. In case of the reaction using complex **1** as catalyst most of the conversion occurs during the first hour of the reaction (∼78%).

The second-generation palladium metallodendrimer, DAB-G2(impyr-PdCl$_2$)$_8$ (**3**), shown in Fig. 4, was also used as a catalyst precursor in the reaction of methyl acrylate

with iodobenzene. Qualitatively, the same order of catalyst activity was found (Fig. 5). Catalyst **3** gave about 92% conversion of iodobenzene in 8 h. It is noted that catalyst **3** showed a lower conversion after 1 h of reaction compared to the first-generation dendrimer **1** after the same amount of time. Obviously, complex **3** needs time to develop full catalytic capacity, as this complex is sterically more bulky than the first-generation. In addition the longer induction period required for **3**, suggests that a relatively longer time is needed for **3** to develop the catalytically active metallic

(2)
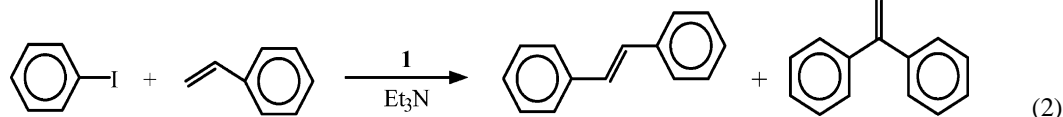
palladium compared to **1**. In addition, diffusion effects of the substrate could also be a limiting factor, as the greater
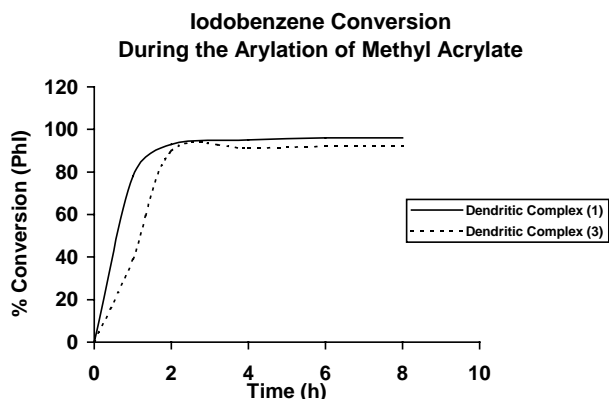
steric bulk and entanglement of the dendritic arms of the second-generation could limit accessibility to the active sites.

3.2. Catalytic reactions with styrene

In the reaction of iodobenzene and styrene, the three palladium sources used in the afore-mentioned Heck reaction, also successfully catalyse this reaction to yield the product, *trans* 1,2-diphenylethylene or stilbene (Eq. (2)).

Two conclusions are apparent from these reactions. Firstly, the rate of consumption of iodobenzene is slower than it was in the methyl acrylate reactions. This is a similar observation to the findings of Heck [23] and other groups. Secondly, the rate of reaction, as was the case with methyl acrylate, is dependent on the nature of the palladium source used to catalyse the reaction. By comparing the rate of consumption of iodobenzene, the catalysts can be arranged in the following order for the conversion of iodobenzene:

dendritic complex **1** > mononuclear complex **2** > $PdCl_2$.

Much lower conversions are observed for $PdCl_2$ (31%) and the mononuclear iminopyridyl complex **2** (47%) over 8 h, in comparison with the dendritic complex **1** (86%) (Fig. 6). It seems that catalyst agglomeration is more pronounced for $PdCl_2$ and the mononuclear complex in this reaction with the less active styrene, than was the case with methyl acrylate. In comparison with the methyl acrylate reaction, the catalyst **1** also shows a lower conversion of iodobenzene. In addition there is a competing side-reaction, in which some polystyrene forms during the reaction. To our knowledge catalytic polymerisation of styrene has not been observed with neutral Pd(II) compounds [24], such as $Pd(PhCN)_2Cl_2$, $PdCl_2$ and $Pd(OAc)_2$, and was not observed in our reaction with $PdCl_2$ either. A small amount of polystyrene was found to form for the mononuclear complex, but the formation of polymer (0.432 g) was more significant using the dendritic complex **1**. This equates to 14% of styrene that is consumed to form polystyrene during the reaction. Since the reaction is conducted in stoichiometric amounts, this value correlates with the 86% conversion of iodobenzene. A control reaction performed with the same substrates under the same conditions, but in the absence of any palladium, revealed no polystyrene formation. This rules out thermal polymerisation of styrene and suggests that the dendritic complex **1**, under correct reaction conditions, could also potentially catalyse the polymerisation of styrene. This finding is currently under further investigation in our lab.

The regio-selectivity of this reaction is also lower compared to that of the methyl acrylate reaction. In this reaction,
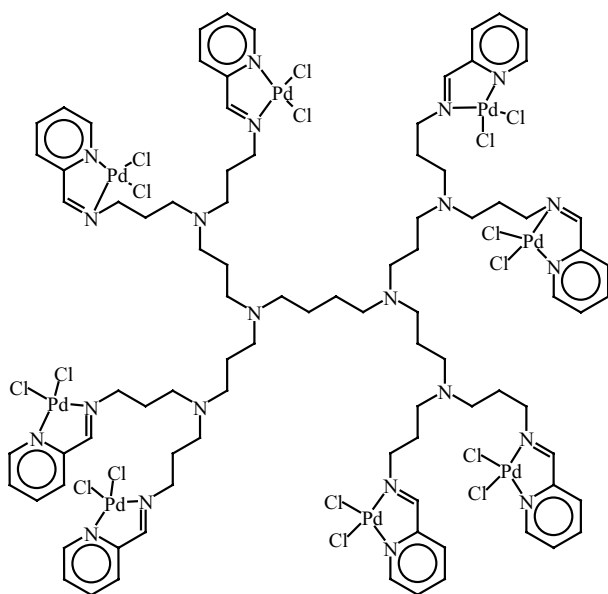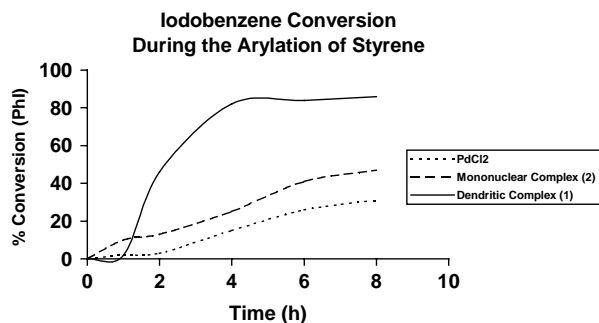
Fig. 4. Second-generation pyridylimine palladium dendrimer (**3**).

Fig. 5. Conversion as a function of time for the arylation of methyl acrylate with iodobenzene.

Fig. 6. Conversion as a function of time for the arylation of styrene with iodobenzene.

a mixture of the β-arylated and α-arylated products was observed, with the β-product being more dominant. As was the case in the methyl acrylate reaction, a small amount of the β,β-disubstituted product was also found.

3.3. Catalytic reactions with 1-octene

The reaction of 1-octene and iodobenzene shows the dendritic complex **1** to be a highly effective Heck catalyst precursor, responsible for a 91% conversion of iodobenzene after 8 h (Fig. 7). However, a mixture of products was obtained (Eq. (3)).
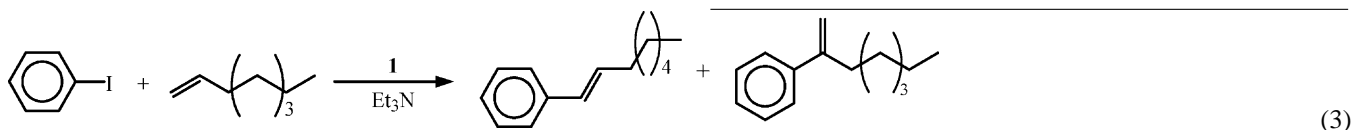
The high conversion of iodobenzene indicates that the dendritic complex **1** is a highly efficient catalyst precursor, capable of coupling iodobenzene with either electron-deficient or electron-rich olefins. This comparison is also drawn with respect to the mononuclear complex and PdCl$_2$, which show a much slower rate of conversion over the same period. However, the use of more electron-donating substituents in the olefin, sees a drastic
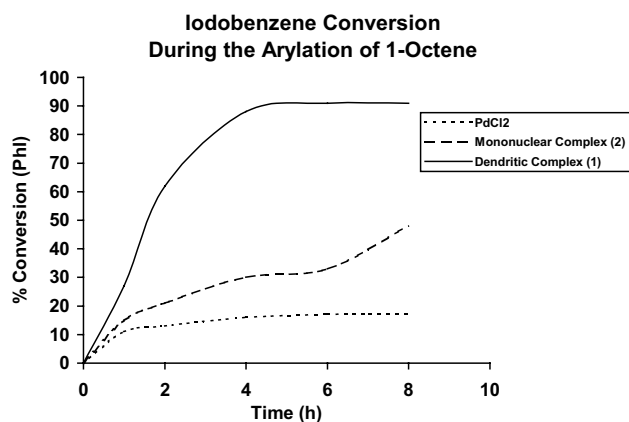
decrease in regio-selectivity, as a mixture of arylated products, *cis/trans* isomers and β,β-disubstituted compounds are formed. This is similar to findings with other catalytic systems reported in the literature [19].

4. Conclusions

The dendritic palladium complex **1** proved to be a very active and efficient catalyst precursor in Heck coupling reactions. The dendritic complex successfully achieved high conversions of iodobenzene, in the coupling of the aryl-halide with electron-deficient or electron-rich olefins. However, electronic factors seem to play a decisive role in determining the regiochemistry of the reaction. Reactions with methyl acrylate, an electron-deficient olefin, yield mainly β-arylated products, whilst the electron-rich olefin, 1-octene, yielded a mixture of arylated products, *cis/trans* isomers and β,β-disubstituted compounds. With respect to catalyst activity, the dendritic complex **1** generally shows a higher conversion and the reactions proceed at a faster reaction rate compared to the mononuclear iminopyridyl-palladium analogue and the palladium salt, PdCl$_2$. Qualitatively, the catalyst activity did not change dramatically on increasing the dendrimer generation. The initial slower conversion of the second-generation metallodendrimer **3** is brought on by the longer induction period required for the catalyst to achieve its full catalytic potential.

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Fig. 7. Conversion as a function of time for the arylation of 1-octene with iodobenzene.

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