

# Cyclopalladated imine catalysts in Heck arylation: search for the catalytic species†

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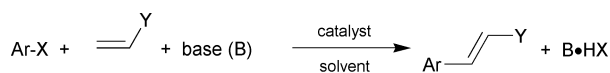
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The application of the new cyclopalladated imine complexes of the Milstein-type **1d**, **2a** and **2b** and the immobilised derivative **2c** in the Heck reaction has provided evidence that these complexes are unstable and the active species is metallic palladium.

The palladium-catalysed reaction of organic halides with alkenes (the Heck reaction, Scheme 1) is a well-established method for carbon–carbon bond formation.<sup>1</sup> The reaction is usually carried out homogeneously in the presence of phosphine ligands and a base.



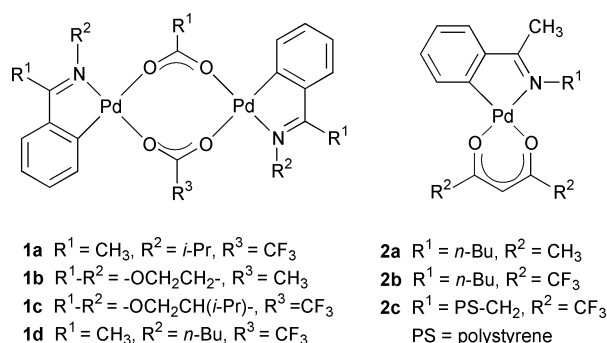
Scheme 1 The Heck reaction.

The need for relatively large amounts of catalyst and the early precipitation of palladium black are severe limitations that have so far prevented widespread industrial application of the Heck reaction. However, thermally robust cyclopalladated complexes offer a way to overcome these stability limitations. Specifically, in addition to the numerous examples that are based on palladated phosphines,<sup>2</sup> the cyclopalladated imine complexes **1a–c** were recently described.<sup>3</sup> Contrary to the ubiquitous application of palladium phosphine complexes as catalysts for the Heck reaction, the use of nitrogen-based catalysts is still very rare. However, these cyclopalladated imines form thermally and air-stable catalysts with high activities (turnover numbers {TON} > 10<sup>6</sup> were achieved).

In order to improve the recyclability, and thereby the applicability, of these highly active cyclopalladated imine catalysts, we attempted to immobilise one of these complexes. Among the numerous attempts to immobilise Pd catalysts on various supports,<sup>4</sup> there is only one example of an immobilisation *via* nitrogen-based tethers.<sup>5</sup> To avoid problems arising from the dimeric nature of catalysts **1a–c**, we utilised Pd(hfac)<sub>2</sub> instead of Pd(OAc)<sub>2</sub> as the source of Pd(II). The monomeric nature of cyclopalladated phosphine complexes bearing acac and hfac counterions has been reported.<sup>2d</sup> To guarantee comparability of results, we also synthesised the homogeneous model complexes **1d**, **2a** and **2b**. All these new palladacycles have been fully characterised.† Additionally, the monomeric nature of **2b** was verified by X-ray analysis (Fig. 1).‡

Utilising commercially available aminomethyl-functionalised polystyrene beads (AMPS, Fluka 81553), the catalyst **2c** was readily prepared in two steps (Scheme 2). A catalyst loading of 0.544 mmol g<sup>-1</sup> was determined by XRF analysis. The characteristic imine C=N stretch vibration of 1661 cm<sup>-1</sup> in the IR spectrum for the imine-functionalised support shifted to 1636 cm<sup>-1</sup> in **2c**. The latter value is in good agreement with that of the homogeneous analogue **2b**.

The catalytic behaviour of the new palladacycles **1d** and **2a–c** was studied in the coupling reaction of iodobenzene with



styrene in *N*-methylpyrrolidinone (NMP). *n*-Pr<sub>3</sub>N was employed as the base in all experiments. In accordance with the results for **1a–c**, all experiments were performed in air. A

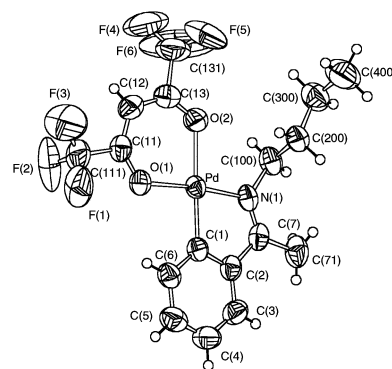
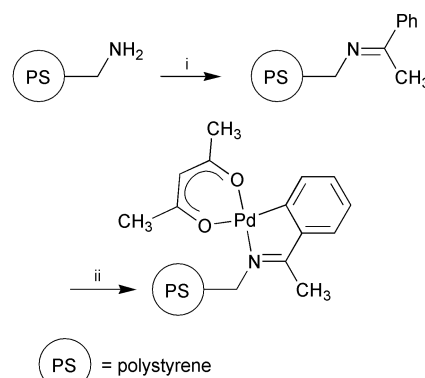


Fig. 1 The molecular structure of **2b**. Relevant bond distances (Å) and angles (°): Pd–C(1) 1.9461(30), Pd–N(1) 1.9788(43), Pd–O(1) 2.0159(46), Pd–O(2) 2.1106(23), N(1)–C(7) 1.2776(42), C(1)–C(2) 1.3808(44), C(2)–C(7) 1.4630(49); N(1)–Pd–C(1) 80.73(13), N(1)–Pd–O(2) 95.68(11), O(1)–Pd–O(2) 89.82(10), O(1)–Pd–C(1) 93.64(12).



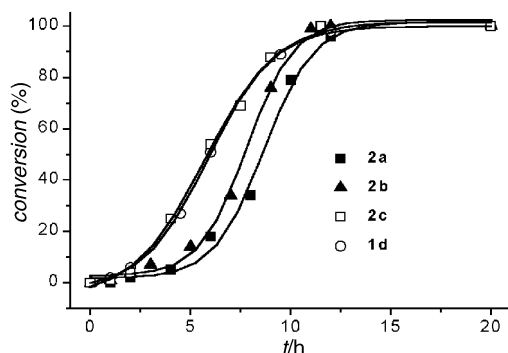
Scheme 2 Reagents and conditions: i, acetophenone (1.1 equiv.), cat. TsOH, toluene, 112 °C, 16 h; ii, Pd(hfac)<sub>2</sub> (0.75 equiv.), C<sub>6</sub>H<sub>6</sub>, 68 °C, 12 h.

† Electronic supplementary information (ESI) available: selected spectroscopic data for **1d**, **2a** and **2b**. See <http://www.rsc.org/suppdata/cc/b0/b004503k/>

**Table 1** Results of the Heck reaction catalysed by imine catalysts **1d** and **2a–c**<sup>a</sup>

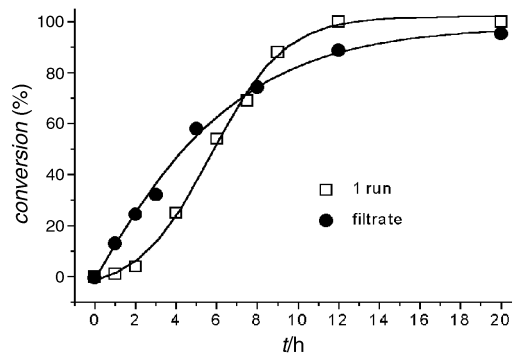
Entry	Catalyst/mmol	Run	T/°C	t/h	Yield (%) <sup>b</sup>	TON
1	<b>2a</b> ( $3.2 \times 10^{-3}$ )	1	100	14	100	1562
2	<b>2b</b> ( $3.2 \times 10^{-3}$ )	1	100	12	100	1562
3	<b>1d</b> ( $3.2 \times 10^{-3}$ )	1	100	12	100	1562
4	<b>2b</b> ( $5 \times 10^{-5}$ )	1	140	120	91	91000
5	<b>2c</b> ( $3.2 \times 10^{-4}$ )	1	140	11	100	15625
6	<b>2c</b> ( $2.8 \times 10^{-4}$ ) <sup>c</sup>	2 <sup>d</sup>	140	20	95	17006
7	<b>2c</b> ( $4.0 \times 10^{-5}$ )	2 <sup>e</sup>	140	40	0	0
8	<b>2c</b> ( $3.2 \times 10^{-3}$ )	1	100	13	100	1562
9	<b>2c</b> ( $4.5 \times 10^{-4}$ ) <sup>c</sup>	2 <sup>d</sup>	100	120	100	11108
10	<b>2c</b> ( $2.7 \times 10^{-3}$ )	2 <sup>e</sup>	100	13	100	1852
11	<b>2c</b> ( $1.9 \times 10^{-3}$ ) <sup>c</sup>	3 <sup>d</sup>	100	18	100	2630
12	<b>2c</b> ( $8.0 \times 10^{-4}$ )	3 <sup>e</sup>	100	40	0	0

<sup>a</sup> Amounts: PhI, 5 mmol; styrene, 6 mmol; *n*-Pr<sub>3</sub>N, 7 mmol; NMP, 5 ml; mesitylene (int. standard), 0.25 ml. <sup>b</sup> Stilbene, *trans/cis* = 6.8–7.4; determined by GC. <sup>c</sup> Determined by AAS analysis. <sup>d</sup> Filtrate of previous run. <sup>e</sup> Recovered **2c** from previous run.

**Fig. 2** Plot of conversion *versus* time for the Heck reaction of iodobenzene with styrene for the cyclopalladated catalysts **1d**, **2a–c** at 100 °C.

control experiment under N<sub>2</sub> with otherwise identical conditions showed no difference in catalyst activity. All catalysts were active under the employed conditions and pure stilbene (*trans/cis* = 6.8–7.4) was obtained (Table 1).

The immobilised catalyst **2c** showed a level of activity in the first run that is comparable to that of the three homogeneous analogues **1d**, **2a** and **2b** (Table 1, entries 1–3, 8). An increase of the reaction temperature from 100 to 140 °C led, as expected, to a rise of several orders of magnitude in TON (entry 2 *cf.* 4). An intriguing feature, which is exhibited by all the new catalysts in their first catalytic runs, is the presence of an induction period of about one hour (Fig. 2). Hence, the catalytically active species is not identical with the originally employed palladacycle, but is only formed during the course of the reaction. The gradual increase of the reaction rate after the initial induction period is indicative of a steady increase of catalyst concentration over the course of the reaction. Further evidence about the nature of the catalytically active species arises from the observation that the immobilised catalyst **2c**, recovered by filtration from an initial catalytic run at 140 °C (Table 1, entry 5), proved to be completely inactive in a consecutive run (entry 7). Instead, the filtrate of the initial run exhibited an undiminished level of activity upon addition of another equivalent of substrates and base (entry 6). Furthermore, the filtrate catalyses the Heck coupling without the occurrence of an induction period (Fig. 3). Therefore the catalytically active species has to be soluble. The imine ligand of the immobilised palladacycle in **2c** cannot be removed from the polystyrene support due to the firm C–C linkage. Hence, the catalytically active species must be formed under loss of this ligand. The liberation of the catalytic species from **2c** is slowed sufficiently at 100 °C to allow some of the catalyst precursor to remain on the support after the first run. Therefore some activity is maintained for a second, but not a third run. Accordingly, the

**Fig. 3** Plot of conversion *versus* time for the Heck reaction of iodobenzene with styrene for **2c** in the first catalytic run at 100 °C and for the filtrate of the former after addition of a second equivalent of substrates and amine base.

filtrates of both the first and second runs exhibit high levels of activity (entry 8–12).

Contrary to the claim of high thermal stability of the cyclopalladated imine complexes **1a–c**, the catalyst precursors **2a–c** and especially **1d** proved to be thermally labile to such an extent that even moderate heating during the synthesis of these palladacycles caused precipitation of some palladium black. The particularly high lability of **1d** corresponds well with the relatively short induction period found in catalytic runs employing this complex (Fig. 2). The expected rapid decomposition of the palladacycles under the conditions of the Heck reaction was proven by the fact that heating **1d** in NMP to 140 °C for 2 h in the absence of substrates and amine base caused complete degradation under formation of Pd black. In accordance with recent observations by Reetz, who detected catalytically active, R<sub>4</sub>N<sup>+</sup>X<sup>-</sup>-stabilised Pd colloids in comparable phosphine-free systems after a similar induction period,<sup>6</sup> we assume that finely divided palladium particles are also the true source of catalytic activity in our system. The stabilising role of R<sub>4</sub>N<sup>+</sup>X<sup>-</sup> may in our system be adopted by the *n*-Pr<sub>3</sub>NH<sup>+</sup>I<sup>-</sup> that is formed in the course of the catalytic cycle. The high activity of the examined cyclopalladated imine catalysts may be ascribed to the formation of Pd(0) nanoparticles in a particularly active form under the applied conditions.

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## Notes and references

‡ Crystal data for **2b**: C<sub>17</sub>H<sub>17</sub>F<sub>6</sub>NO<sub>2</sub>Pd, *M* = 484.74, triclinic, space group *P*1̄ *a* = 8.314(6), *b* = 9.565(5), *c* = 12.293(4) Å, α = 77.57(7), β = 87.72(4), γ = 79.55(14)°, *U* = 938.8(10) Å<sup>3</sup>, λ = 0.71073 Å, *Z* = 2, *D*<sub>c</sub> = 1.725 Mg m<sup>-3</sup>, *T* = 293 ± 2 K, μ(Mo-Kα) = 1.057 mm<sup>-1</sup>, θ<sub>max</sub> = 30.26°. Structure solved by Patterson technique. Full matrix least squares refinement on *F* to final *R* = 0.059 (*R*<sub>w</sub> = 0.037) for all 5559 reflections and to *R* = 0.037 (*R*<sub>w</sub> = 0.037) for the 4486 reflections with *F* > 2.5σ(*F*). CCDC 182/1754. See <http://www.rsc.org/suppdata/cc/b0/b004502k/> for crystallographic files in .cif format.

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