

Highly active Pd^{II} cyclometallated imine catalysts for the Heck reaction

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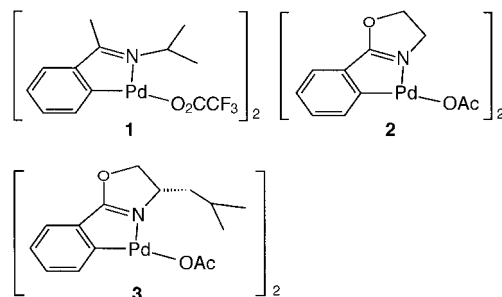
The new cyclopalladated, phosphine-free imine complexes **1–3** are exceptional catalysts for the Heck arylation, leading to more than a million turnovers in some cases; the catalysts are very thermally and air stable and are recovered unchanged after the catalysis.

The Heck arylation of alkenes [eqn. (1)] is a useful synthetic method that is attracting much current interest.¹ Normally, palladium phosphine complexes are utilized, and the reactions



are conducted under an inert atmosphere. Recently, very efficient catalysis using palladium complexes incorporating cyclometallated phosphines,^{2,3} chelating diphosphines,⁴ carbene ligands⁵ and dimethylglycine^{6†} have been reported. We have reported that palladium complexes of tridentate PCP-type ligands are excellent catalysts, and have provided evidence which renders the traditional Pd⁰/Pd^{II} cycle unlikely in that case.⁶ The issue of a possible Pd^{II}/Pd^{IV} cycle in Heck catalysis is currently under debate,^{4,7,8} and a new mechanism involving Pd^{IV} intermediacy in Heck catalysis has been suggested.⁹

We report here¹⁰ that the palladium imine complexes **1–3** are outstanding catalysts for this reaction with turnover numbers



(TON) of more than 10^6 in some cases. These readily prepared Pd^{II} catalysts are exceedingly thermally stable and are not sensitive to oxygen. The use of phosphine free, nitrogen-based ligands in the Heck reaction is very rare and was reported for bidentate nitrogen ligands. However, low catalytic activity was observed.^{11‡}

The new dimeric imine complexes **1–3** in which the metal center is stabilized by a five-membered ring, were readily prepared by treatment of Pd(O₂CCF₃)₂ or Pd(OAc)₂ with the corresponding imines in THF.§ X-Ray analysis (Fig. 1)¶ X-Ray structures of other palladated imine complexes were reported.¹²

Complexes **1–3** show extremely high activity in the catalytic arylation of olefins with aryl iodides and bromides (Table 1). Because of the stabilizing metallated ligand system, the complexes are very thermally stable and no degradation is observed under the reaction temperatures. These complexes are also not sensitive to oxygen and moisture and the reactions can be carried out in air, with no change in efficiencies or yield. The catalyst remains highly active after the reaction is complete, and

upon addition of more substrates catalysis is resumed. At the end of the catalysis, the acetate or trifluoroacetate moieties are substituted to give the corresponding palladiumhalide complex. Conveniently, catalyst **1** can be formed *in situ* under the reaction conditions from Pd(OAc)₂ and the readily available imine ligand, leading to similar results.

While very high TONs and yields are observed for catalysts **1–3**, complex **1** exhibits higher turnover rates. Of the solvents tested, *N*-methylpyrrolidone (NMP) was found to be the best. The reaction can be carried out also in solvents of lower polarity (dioxane) or non-polar ones (mesitylene), although at lower rates. Pure solvent and starting materials should be used in the highly catalytic reactions. Both Na₂CO₃ and NEt₃ were used as bases, although the reaction was faster with the soluble amine, leading to a turnover rate of *ca.* $8 \times 10^4 \text{ h}^{-1}$ and 100% yield with iodobenzene and methyl acrylate.

In a typical experiment, a slight excess of the olefin is added to a solution of the aryl halide in freshly distilled NMP, followed by addition of an equimolar amount of NaHCO₃ or NEt₃. The catalyst is added and the mixture is stirred at 140 °C for the specified time. The reaction mixture is analyzed by gas chromatography and is worked up by addition of water and extraction of the organic phase with CH₂Cl₂. After evaporation of the volatiles, the essentially pure product is characterized by NMR and IR spectroscopy. Selected results are listed in Table 1.

As expected, the reaction outcome depends on the halide and on the olefin. With iodobenzene and methyl acrylate, essentially complete conversions are obtained with very high turnover numbers of up to 1.4×10^6 , which are among the highest observed so far.|| Methyl crotonate and styrene also react normally, while significantly lower rates are obtained with non-activated alkenes. Chlorobenzene was only marginally reactive.^{13**} The observed TON of 137 100 in the case of bromobenzene is similar to the one that we reported for PCP-type ligands⁶ but the reaction was slower in the latter case. As

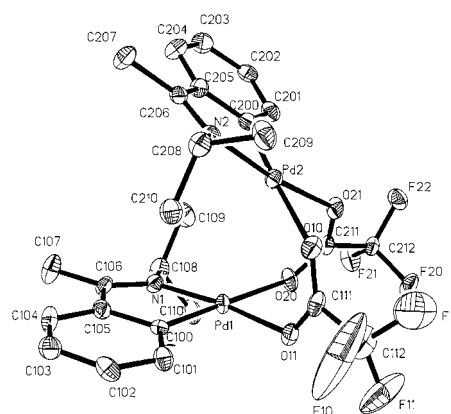


Fig. 1 Perspective view (ORTEP) of complex **1**. Bond distances (Å) and angles (°) (errors in last digits in parentheses) are: Pd(1)–C(100) 1.942(6); Pd(1)–N(1) 2.035; Pd(1)–O(11) 2.065(5); Pd(1)–O(20) 2.174(4); N(1)–C(106) 1.295(8); C(100)–C(105) 1.422(9); C(105)–C(106) 1.450(9); C(100)–Pd(1)–N(1) 81.0(2); C(100)–Pd(1)–O(11) 92.7(2); C(100)–Pd(1)–O(20) 178.3(2).

Table 1 Results of the Heck reaction with the imine catalyst 1–3

ArX ^a	Alkene ^a	Solvent ^b	Base	Catalysts (mmol/10 ⁻⁵)	t/h	T/°C	TON	Yield (%) ^c
PhI	methyl acrylate	NMP	Na ₂ CO ₃	1 (3.5)	9	140	142900	100 ^d
PhI	methyl acrylate	Dioxane	Na ₂ CO ₃	1 (3.5)	40	140	36900	25 ^d
PhI	methyl acrylate	NMP	NEt ₃	1 (3.5)	1	140	142900	100 ^d
PhI	methyl acrylate	DMA	NEt ₃	1 (3.5)	16	140	93700	66 ^d
PhI	methyl acrylate	Dioxane	NEt ₃	1 (3.5)	16	140	107200	75 ^d
PhI	methyl acrylate	Mesitylene	NEt ₃	1 (3.5)	16	140	130300	93 ^d
PhI	methyl acrylate	NMP	Na ₂ CO ₃	1 (0.46)	32	140	1087000	100 ^d
PhI	methyl acrylate	NMP	NEt ₃	1 (0.35)	18	140	1429000	100 ^d
PhI	styrene	NMP	Na ₂ CO ₃	1 (3.5)	80	140	105700	74 ^e
PhI	methyl crotonate	NMP	Na ₂ CO ₃	1 (3.5)	39	140	140000	98 ^f
4-MeO-C ₆ H ₄ I	methyl acrylate	NMP	Na ₂ CO ₃	1 (3.5)	12	140	138600	97 ^g
PhBr	methyl acrylate	NMP	Na ₂ CO ₃	1 (3.5)	43	140	137100	96 ^d
4-CHO-C ₆ H ₄ I	methyl acrylate	NMP	Na ₂ CO ₃	1 (3.5)	25	140	140000	98 ^h
PhI	methyl acrylate	NMP	Na ₂ CO ₃	2 (3.5)	22	140	142900	100 ^d
PhI	methyl acrylate	NMP	Na ₂ CO ₃	3 (3.5)	22	140	142900	100 ^d
PhI	dihydropyran	NMP	Na ₂ CO ₃	3 (70)	68	120	4300	60 ⁱ
PhI	indene	NMP	Na ₂ CO ₃	3 (70)	115	120	5100	72 ^j
PhI	cyclohexene	NMP	Na ₂ CO ₃	3 (70)	68	120	3000	42 ⁱ
PhI	dihydrofuran	NMP	Na ₂ CO ₃	3 (70)	22	140	7100	100 ⁱ
PhI	dihydrofuran	NMP	NEt ₃	3 (10.5)	24	120	38100	80 ⁱ
PhBr	methyl acrylate	NMP	Na ₂ CO ₃	2 (7.0)	130	140	132900	93 ^d

^a Amounts: ArX, 5 mmol; alkene, 6 mmol; Na₂CO₃, 3.5 mmol; NEt₃ 7 mmol. ^b NMP = *N*-methylpyrrolidone; DMA = *N,N*-dimethylacetamide. ^c Determined by GC, based on the aryl halide. ^d Methyl *trans*-cinnamate. ^e Stilbene, *cis*:*trans* = 1:7. ^f Methyl *trans*-3-methylcinnamate:methyl *cis*-3-methylcinnamate:3-methylenebenzenepropanoic acid methyl ester:methyl 4-phenylbut-2-enoate (10:1:1:1). ^g Methyl *trans-p*-methoxycinnamate. ^h Methyl *trans-p*-formylcinnamate. ⁱ Mixture of isomers of the phenyl derivatives of the olefins. ^j Mixture of isomers, main product: 2-phenylindene.

far as we are aware, our results with the relatively inactive bromobenzene and the commonly used acrylate esters are unsurpassed.

In summary, the metallated imine palladium(II) complexes show exceedingly high catalytic activity and yields in the Heck reaction, including reactions of the non-activated bromobenzene. The activities observed are among the highest reported for the Heck reaction. The new catalyst system is very thermally and air stable. Further investigations aimed at clarification of the scope and mechanism of these reactions are in progress.

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Notes and references

† The role of the dimethylglycine additive is unclear and stabilized palladium colloids may be involved in this case. See ref. 6.

‡ With phenanthroline ligands, only 40 TON or less were obtained. Bipyridine and bis-oxazoline ligands were inactive with methyl acrylate and resulted in very low yields and turnovers with other alkenes. See ref. 11.

§ 1: δ_H(C₆D₆) 0.85, 1.15 (d, ³J_{HH} 6.6, 3H, CH₃), 1.06 (s, 3H, CH₃), 3.20 (sept, ³J_{HH} 6.6, 1H, CH), 6.46, 7.29 (m, 1H, H_{aryl}), 6.77 (m, 2H, H_{aryl}); δ_C(C₆D₆) 14.0, 20.8, 21.9, 54.4 (s, CH/CH₃), 116.8 (q, J_{CF} 288, CF₃), 124.3, 126.7, 129.6, 132.5 (s, C_{aryl}), 166.0 (q, ²J_{CF} 38, OC=O), 179.2 (s, C=N). For 2: δ_H(C₆D₆) 2.22 (s, 3H, CH₃), 2.62, 2.82, 3.00, 3.24 (m, 1H, CH₂), 6.71, 6.84 (m, ³J_{HH} 7.6/7.4, 1H, H_{aryl}), 7.01 (d, ³J_{HH} 7.4, 1H, H_{aryl}), 7.48 (d, ³J_{HH} 7.6, 1H, H_{aryl}); δ_C(C₆D₆) 24.5 (s, CH₃), 49.6, 69.7 (s, CH₂), 123.4, 125.1, 130.1, 132.1, 131.8, 149.2 (s, C_{aryl}), 174.4 (s, C=N), 181.1 (s, OC=O). For 3: δ_H(C₆D₆) 0.70 (d, ³J_{HH} 6.6, 6H, CH₃), 0.84 (m, 1H, left part of CH₂), 1.14 (m, 1H, CH), 1.82 (ddd, 1H, right part of CH₂), 2.16 (s, 3H, CH₃), 3.09 (m, 1H, CH), 3.37 (m, 2H, CH₂), 6.75 (t, ³J_{HH} 7.6, 1H, H_{aryl}), 6.87, 7.13 (m, ³J_{HH} 7.6, 1H, H_{aryl}), 7.50 (d, ³J_{HH} 7.6, 1H, H_{aryl}); δ_C(C₆D₆) 21.8, 23.5, 24.6, 25.2 (s, CH/CH₃), 43.5, 75.5 (s, CH₂), 60.4 (s, CH), 123.5, 125.2, 130.2, 132.0, 132.4, 149.3 (s, C_{aryl}), 173.2 (s, C=N), 181.1 (s, OC=O).

¶ Crystal data for 1: C₂₆H₂₈N₂O₄F₆Pd₂, *M* = 759.30, yellow, plates, 0.2 × 0.2 × 0.05 mm³, monoclinic, *P*2(1)/*c* (No. 14), *a* = 17.044(3), *b* = 16.976(3), *c* = 19.725(4) Å, β = 97.75° (3), from 25 reflections, *T* = 110 K, *V* = 5655(2) Å³, *Z* = 8, *D_c* = 1.784 Mg m⁻³, μ = 1.346 mm⁻¹, Mo-Kα, 12993 independent reflections, *R_{int}* = 0.0481, final *R*₁ = 0.0618, CCDC

182/1144. Crystallographic data are available in .cif format from the RSC web site, see: <http://www.rsc.org/suppdata/cc/1999/357>

|| As far as we are aware, this is the highest TON reported for a quantitative Heck reaction. A TON of 1120000 was reported for the reaction of iodobenzene with methyl acrylate after 13 days at 95 °C, but the yield was 56%. See ref. 3.

** Catalysis with chlorobenzene was accomplished by addition of NaI and NiBr₂. However, the reaction was very slow, resulting in 10% yield and 190 TON after 21 h at 140 °C.

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