# Chelating diphosphine–palladium(II) dihalides; outstandingly good catalysts for Heck reactions of aryl halides

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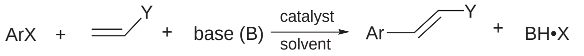
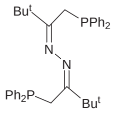
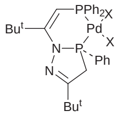
**Contrary to previously held views, chelating diphosphine–palladium dihalide complexes are excellent catalysts for Heck reactions involving aryl halides; the undesirability of trying to prepare such catalysts *in situ* is discussed.**

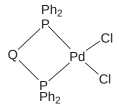
The Heck vinylation or olefination reaction [eqn. (1)] is very important in organic synthesis.[1a–c] A Heck catalyst is frequently generated *in situ* from $Pd(OAc)_2$ and a tertiary phosphine, L = $PPh_3$ or P(*o*-tolyl)$_3$; commonly 1–5 mol% of Pd is used which means that the maximum turnover numbers are only 100–20. When discussing arylation with aryl halides[1b] Heck stated that 'chelating diphosphines do not give as good catalysts'; this was in comparison with the catalysts commonly used and mentioned above and which are therefore a benchmark for comparing reactivity and performance. Cabri and co-workers[2a] agreed with this statement of Heck and in a review[2b] wrote that his statement 'Chelating diphosphines...in general do not produce useful catalysts' was valid only because aryl halides were used but also wrote 'with bidentate ligands a decrease in reaction rates or sometimes a complete suppression of the reaction is observed'. Ditertiary phosphine–palladium complexes are effective catalysts for Heck reactions with aryl triflates or with aryl halides in the presence of a halide scavenger (Ag or Tl).[1c,2a–c] Overman and coworkers have demonstrated that diphosphine (*e.g.* BINAP)–Pd catalysts promote intramolecular Heck reactions with aryl iodides, with high ee.[2c] However, very large amounts of catalyst, 3–10 mol%, have been used for these reactions. The prevailing belief is that chelating diphosphine–Pd complexes are not good catalysts for the classical Heck reaction [eqn. (1)].

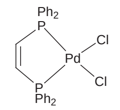

(1)

We have now investigated **2a** and **2c** and ditertiary phosphine–palladium(II) dihalide complexes **3a–d** and **4** and find them to be outstanding as catalysts for Heck olefination reactions with aryl iodides and bromides in several respects. Our results are summarised in Table 1. High yields and very high turnover numbers (TONs; up to 225 000) were obtained, with good rates; catalysts were active over the temperature range 50–150 °C, which could probably be extended; in some cases reaction times could probably be reduced, we left some reactions for prolonged times to show that the catalysts were stable; in no case was any metallic Pd produced. The yields were isolated yields and chromatography was not necessary, the Pd being removed by a simple wash with a very small amount of aqueous sodium cyanide solution and the product was then purified by crystallisation. We have used this very effective isolation procedure for Heck reactions catalysed by palladacycles.[3] The very stable complex **2a** can be easily made in high yield, from **1** and $[PdCl_2(NCPh)_2]$[4] by a transannular reaction; we also reported the crystal structure of **2b** and prepared **2c** by metathesis.[4] Treatment of PhI (2.0 g, 10 mmol), styrene and $NBu^n_3$ with catalyst **2a** (0.044 mg) in dmf at 95 °C for 12 d gave a pale orange solution. This was taken up in $CH_2Cl_2$ and after a water wash and then a wash with a solution of NaCN (2 mg) in water the organic layer was essentially colourless. The stability constant for $[Pd(CN)_4]^{2-}$ is about $10^{52}$,[5] and this wash presumably took the Pd into the aqueous layer. Crystallisation from methanol then gave *trans*-stilbene in 67% yield corresponding to a TON of 101 200. The other reaction mixtures summarised in Table 1 were worked up in an analogous manner, except that for reactions with methyl acrylate the work up was done in diethyl ether. In example 2, with 9 days reaction time at 95 °C, the isolated yield of methyl cinnamate was 92%, TON = 139 000. We also studied catalyst **2a** at higher temperatures, 125 and 150 °C, and shorter reaction time (48 h, entries 4 and 5) with very good yields and excellent TONs (110 200 and 60 400) and no sign of decomposition to metallic Pd. Bromide **2c** was a good catalyst for converting methyl acrylate and iodobenzene into methyl cinnamate (example 3). **2a** catalysed the olefination of 4-bromoacetophenone to acetylstilbene; 91% yield, TON = 27 500. Bases other than $NBu^n_3$ were used, entries 7–10, *viz.* NaOAc, $K_2CO_3$ with $NBu^n_4Cl$, $K_2CO_3$ or $KHCO_3$, in example 8 a reaction temperature of only 50 °C was used. Reaction 11, with 4-bromocyanobenzene was carried out at 125 °C for 12 h. Products were identified by their proton NMR spectra.


**1**


X = Cl **2a**, I **2b**, Br **2c**


Q = $(CH_2)_n$; *n* = 1 **3a**, 2 **3b**, 3 **3c**, 4 **3d**


**4**

The 4-membered ring chelated dppm complex **3a**[6,7] (0.032 mg) converted PhI (1 g) plus styrene into stilbene at 150 °C/48 h in 87% yield with a TON of 76 300 and no sign of decomposition. **3a** also converted 4-bromoacetylbenzene into 4-acetylstilbene at 125 °C in 88% yield. The 5-membered chelate ring complex catalysts **3b**[8] and **4**[9] gave very good yields (76% to 95%) of stilbene derivatives and **4** gave acetylstilbene in 82% yield, using $KHCO_3$ as base. The 6-membered ring chelate **3c** gave a particularly high TON (224 700) and 80% yield for the conversion of iodobenzene/styrene to stilbene, with reaction conditions 3 d/125 °C; the 7-membered chelate dppb complex **3d** under these conditions gave a TON of 170 300. **3c** and **3d** also catalysed reactions of 4-bromoacetylbenzene with styrene in high yields and with good TONs. We favour a mechanism for the syntheses summarised in Table 1 involving a $Pd^{II}$–$Pd^{IV}$ cycle similar to those we proposed for Heck reactions catalysed by palladacycles or in the phosphine free systems (Jeffery conditions).[3,10]

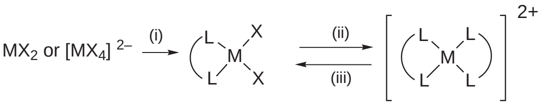
Typically, in Heck syntheses involving chelating diphosphines, the diphosphine and the equivalent amount of palladium, *e.g.* palladium acetate, has been added to the mixture of reactants in the belief that a compound of type $[(L–L)PdX_2]$[2b] will form *in situ*. However, there are very good reasons for

**Table 1** Selected results of the Heck reactions catalysed by P–P palladium chelates[a]

| No. | Aryl halide | Olefin | ArX/olefin mmol/mmol | Catalyst (mmol) | Time ($T$/°C) | Yield (%) (TON) |
|---|---|---|---|---|---|---|
| 1 | PhI | sty | 10/15 | **2a** ($6.6 \times 10^{-5}$) | 12 d (95 °C) | 67 (101000) |
| 2 | PhI | mac | 10/15 | **2a** ($6.6 \times 10^{-5}$) | 9 d (95 °C) | 92 (139000) |
| 3 | PhI | mac | 10/15 | **2c** ($4.6 \times 10^{-3}$) | 24 h (95 °C) | 81 (1760) |
| 4 | PhI | sty | 10/15 | **2a** ($6.6 \times 10^{-5}$) | 48 h (125 °C) | 73 (110200) |
| 5 | PhI | sty | 5/7.5 | **2a** ($6.6 \times 10^{-5}$) | 48 h (150 °C) | 80 (60400) |
| 6 | bab | sty | 2/3 | **2a** ($6.6 \times 10^{-5}$) | 66 h (125 °C) | 91 (27500) |
| 7[b] | PhI | sty | 2/3 | **2a** ($1.7 \times 10^{-2}$) | 20 h (95 °C) | 69 (81) |
| 8[c] | PhI | mac | 10/15 | **2a** ($5 \times 10^{-2}$) | 42 h (50 °C) | 68 (136) |
| 9[d] | bab | sty | 10/15 | **2a** ($1.08 \times 10^{-2}$) | 40 h (125 °C) | 85 (787) |
| 10[e] | bab | sty | 10/15 | **2a** ($1.08 \times 10^{-2}$) | 30 h (125 °C) | 76 (703) |
| 11 | bcb | sty | 2/3 | **2c** ($4.6 \times 10^{-3}$) | 12 h (125 °C) | 75 (326) |
| 12 | PhI | sty | 5/7.5 | **3a** ($5.7 \times 10^{-5}$) | 48 h (150 °C) | 87 (76300) |
| 13 | bab | sty | 10/15 | **3a** ($5.8 \times 10^{-3}$) | 24 h (125 °C) | 88 (1520) |
| 14 | bab | sty | 10/15 | **3b** ($6 \times 10^{-3}$) | 24 h (125 °C) | 87 (1450) |
| 15[e] | bab | sty | 10/15 | **4** ($5.2 \times 10^{-3}$) | 24 h (125 °C) | 82 (1580) |
| 16 | PhI | sty | 10/15 | **3c** ($3.56 \times 10^{-5}$) | 3 d (125 °C) | 80 (224700) |
| 17 | bab | sty | 2/3 | **3c** ($9.3 \times 10^{-3}$) | 24 h (125 °C) | 75 (161) |
| 18 | PhI | sty | 10/15 | **3d** ($3.64 \times 10^{-5}$) | 3 d (125 °C) | 62 (170300) |
| 19 | bab | sty | 2/3 | **3d** ($3 \times 10^{-4}$) | 24 h (125 °C) | 79 (5270) |

[a] For all except examples 7–10 and 15, 1.2 equiv. $NBu^n_3$ to the aryl halide were used as base; dmf was used as solvent to dissolve the catalyst, *e.g.* in examples 6, 11, 17 and 19, 1 cm$^3$ of dmf was used; in examples 1–5, 12, 16 and 18, 2 cm$^3$; in examples 9, 13, 14 and 15, 5 cm$^3$; in examples 8 and 10, 10 cm$^3$. sty = styrene, mac = methyl acrylate, bab = 4-bromoacetylbenzene, bcb = 4-bromocyanobenzene. [b] $NaOAc \cdot 3H_2O$ (2.65 mmol) used as base. [c] $K_2CO_3$ (25 mmol, base) and $Bu^n_4NCl$ (10 mmol) were used. [d] $K_2CO_3$ (15 mmol) used as base. [e] $KHCO_3$ (25 mmol) used as base.

thinking that in some cases only a fraction of the Pd will do this. In Pd$^{II}$ and Pt$^{II}$ chemistry, in many cases, on addition of one equivalent of a chelating diphosphine or diarsine to $[MX_4]^{2-}$, half of the Pd$^{II}$ or Pt$^{II}$ is converted into $[M(L–L)_2]^{2+}$, *i.e.* in eqn. (2) half the metal will remain as $[MX_4]^{2-}$.[12a–d] This follows from the very high *trans*-effect (*trans*-labilising effect) of a tertiary phosphine (arsine) compared with a chloride ligand. We showed that a chloride ligand *trans* to a tertiary phosphine such as $PEt_3$ was substituted by pyridine about $10^4$ times faster than chloride *trans* to another chloride ligand,[11] *i.e.* in eqn. (2) the rate of substitution (ii) will be much greater than that of substitution (i). Thus a Magnus type salt $[M(L–L)_2][MX_4]$ is formed, which is often of very low solubility. Conversion of such a salt to *cis*-$[(L–L)MX_2]$ is often difficult; boiling it in dmf (bp 153 °C) or with a mixture of hydrochloric acid and ethanol will often effect the conversion[12a–c] but in some cases even such extreme conditions are not sufficient or satisfactory.[12c,d] A satisfactory method of synthesising complexes of type $[(L–L)PdX_2]$ is to treat a compound of type $[PdX_2(NCR)_2]$, *e.g.* the well known $[PdCl_2(NCPh)_2]$, with the chelating diphosphine in a suitable solvent system, *e.g.* $CH_2Cl_2$ or acetone,[12a–d] and this is the method we have used in the present work. Complexes **3a–d** and **4** have been studied extensively[6–9,12a–d] and **3a–c** have had their crystal structures determined.[7]



(2)

As will be gathered from the above, process (iii) in eqn. (2) may be exceedingly slow and it is not known in detail how it occurs. Palladium acetate is a trimer, the acetate ligand is labile and one might expect that on adding a chelating diphosphine and the equivalent amount of palladium acetate to a mixture of reactants for a Heck synthesis, *in situ*, much of the Pd would be converted into $[Pd(L–L)_2]^{2+}$ but not much $[(L–L)PdX_2]$ (X = OAc *etc.*) would be formed. If so it calls into question some arguments which have been put forward when discussing Heck reactions involving Pd–chelating diphosphine catalysts.[2b,c] It is recommended that catalysts for Heck reactions should be preformed and the source of Pd and the phosphine not added separately to the reactants; this could become especially important when very small amounts of Pd and diphosphine are used.

Even when catalysts are generated from a Pd$^0$ complex, such as $Pd_2(dba)_3$, the resultant complex(es) will oxidatively add aryl halide to give Pd$^{II}$ complexes which could then participate in a catalytic cycle involving Pd$^{II}$/Pd$^{IV}$.

## Notes and References

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1 (*a*) R. F. Heck, *Palladium Reagents in Organic Synthesis*, Academic Press, London, Benchtop Edition, 1990; (*b*) R. F. Heck, *Vinyl Substitution with Organopalladium Intermediates*, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon, Oxford, 1991, vol. 4, p. 833; (*c*) A. de Meijere and F. E. Meyer, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 2379.

2 (*a*) W. Cabri, I. Candiani and A. Bedeschi, *J. Org. Chem.*, 1992, **57**, 3558; (*b*) W. Cabri and I. Candiani, *Acc. Chem. Res.*, 1995, **28**, 2; (*c*) L. E. Overman and D. J. Poon, *Angew. Chem.*, 1997, **36**, 518.

3 B. L. Shaw, S. D. Perera and E. A. Staley, *Chem. Commun.*, 1998, 1361.

4 S. D. Perera, B. L. Shaw and M. Thornton-Pett, *J. Chem. Soc., Dalton Trans.*, 1993, 3653.

5 M. T. Beck, *Pure Appl. Chem.*, 1987, **59**, 1703.

6 W. L. Steffen and G. J. Palenik, *Inorg. Chem.*, 1976, **15**, 2432.

7 D. W. Meek, P. E. Nicpon and V. I. Meek, *J. Am. Chem. Soc.*, 1970, **92**, 5351.

8 G. Booth and J. Chatt, *J. Chem. Soc. (A)*, 1966, 634.

9 D. J. Gulliver, W. Levason and K. G. Smith, *J. Chem. Soc., Dalton Trans.*, 1981, 2153.

10 B. L. Shaw, *New J. Chem.*, 1998, **22**, 77.

11 F. Basolo, J. Chatt, H. B. Gray, R. G. Pearson and B. L. Shaw, *J. Chem. Soc.*, 1961, 2207.

12 (*a*) A. T. Hutton and C. P. Murray, in *Comprehensive Coordination Chemistry*, ed. G. Wilkinson, R. D. Gillard and J. A. McCleverty, vol. 5, p. 1162; (*b*) C. A. McAuliffe and W. Levason, *Phosphine, Arsine and Stibine Complexes of the Transition Elements*, Elsevier, Amsterdam, 1979; (*c*) J. Chatt and F. G. Mann, *J. Chem. Soc.*, 1939, 1622; (*d*) M. J. Hudson, R. S. Nyholm and M. H. B. Stiddard, *J. Chem. Soc.*, 1968, 40.

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