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Orthopalladated triarylphosphite complexes as highly efficient catalysts in the Heck reaction

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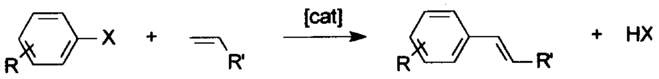
Abstract. An orthopalladated complex of commercially available tris(2,4-di-*tert*-butylphenyl)phosphite proves to be an extremely active catalyst in the Heck arylation of alkenes, with turnover numbers of up to 5,750,000 (mol product.mol Pd^{-1}) and turnover frequencies of up to nearly 300,000 (mol product.mol $Pd^{-1}.h^{-1}$).

Keywords: Heck reactions; metalation; palladium and compounds; catalysis

The exploitation of orthometallated triarylphosphite complexes in catalysis has so far been limited to a few reductions[1,2] and only two examples of catalytic C-C bond formation.[3,4] An important class of C-C bond forming reactions is the Heck arylation of alkenes (Scheme 1). Generally, this reaction requires fairly high catalyst concentrations (1-10mol%) limiting its attractiveness to large scale commercial applications. Consequently there has recently been an interest in developing high activity catalysts that can be used in low concentrations.

Scheme 1



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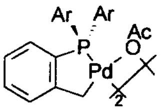
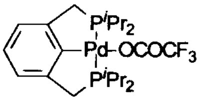
Herrmann has reported the use of the Pd(II) complex **1** with metallated tris(2-methylphenyl)phosphine and related compounds as highly efficient catalysts for this reaction.[5] Similarly, the orthopalladated complex **2** and related species have recently been shown to be active catalysts,[6] as have palladacyclic trinapthylphosphine complexes.[7] We have recently demonstrated that the orthopalladated triarylphosphite complex **3** is an extremely active catalyst in Suzuki and Stille biaryl coupling reactions giving for the first time turnover numbers (TONs) of up to 1,000,000 (mol product.mol Pd^{-1}) and turnover frequencies (TOFs) of over 800,000 (mol product.mol $Pd^{-1}.h^{-1}$).[4] We report here the application of **3** to the Heck reaction. For comparison purposes we also investigated the use of the triphenylphosphine adduct of **3**, **4**, and the previously reported orthopalladated dimethylbenzylamine complex **5**.[8]



Ar = 2-MeC_6H_4

1



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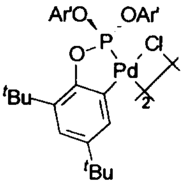

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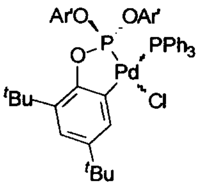
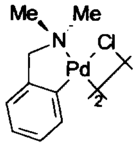


Ar′ = $2,4\text{-}^t\text{Bu}_2\text{C}_6\text{H}_3$

4



5

Representative preliminary results for the use of **3**, **4** and **5** in the coupling of aryl bromides with *n*-butylacrylate and styrene are summarised in table 1. Examining the coupling between butylacrylate and 4-bromoacetophenone we make the following observations. Catalytic activity becomes evident at about 110°C when sodium acetate is employed as the base and increases significantly with temperature, giving TONs of up to 1,000,000 and maximum TOFs of up to at least 190,000. The use of triethylamine as base inhibits catalytic activity up to 140°C, however, activity is restored if the temperature is increased. A highly surprising result is that **3** catalyses the coupling even under air, albeit with somewhat reduced activity, demonstrating that this is a very robust system.

The highest activity was observed in the coupling of 4-bromoacetophenone with styrene with turn over frequencies of up to 290,000 observed and turn over numbers of up to 5.75 million. The previous highest TON for any Heck reaction was 1.12 million in the coupling of iodobenzene with methylacrylate.[7] Substantial quantities of polystyrene are formed during this reaction suggesting a competing process. Indeed in the absence of 4-bromoacetophenone, a mixture of **3** and sodium acetate was found to catalyse oligostyrene formation. This is not an unprecedented phenomenon - orthometallated triarylphosphite ruthenium complexes have also been shown to catalyse oligostyrene formation.[3]

Table 1

Heck arylation of alkenes catalysed by orthopalladated triarylphosphite and arylamine complexes[a]

Aryl bromide	alkene	Catalyst (mol% Pd)	Base	T (°C)	Time (hrs)	Conversion (%)[b]	TON (mol product/mol Pd)
4-bromoacetophenone	butylacrylate	3(0.2)	NaO_2CCH_3	110	1	2	10
4-bromoacetophenone	butylacrylate	3(0.2)	NaO_2CCH_3	140	1	42	210
					20	100	500
4-bromoacetophenone	butylacrylate	3(0.2)	NaO_2CCH_3	180[c]	1	100	500
4-bromoacetophenone	butylacrylate	3(0.2)	NEt_3	140	1	0	0
				180[c]	1	94	470
4-bromoacetophenone	butylacrylate[d]	3(0.0001)	NaO_2CCH_3	180[c]	1	5	50,000
					2	24	240,000
					6	100	1,000,000
4-bromoacetophenone	butylacrylate	3(0.2)	K_2CO_3	140	1	46	230
					18	100	500
4-bromoacetophenone	styrene	3(0.2)	NaO_2CCH_3	140	1	63	315
					24	100	500
4-bromoacetophenone	styrene	3(0.0001)	NaO_2CCH_3	180[c]	1	29	290,000
					21	96	960,000
4-bromoacetophenone	styrene	3(0.00001)	NaO_2CCH_3	180[c]	69	57.5[e]	5,750,000
bromobenzene	butylacrylate	3(0.2)	NaO_2CCH_3	140	18	51	255
4-bromoanisole	butylacrylate	3(0.2)	NaO_2CCH_3	140	10	6	30
4-bromoanisole	butylacrylate	3(0.2)	NaO_2CCH_3	180[c]	1	14	70
					19.5	75	375
4-bromoanisole	butylacrylate	3(0.2)	K_2CO_3	160	1	22	110
					18	88	440
4-bromoanisole	butylacrylate	3(0.01)[f]	K_2CO_3	160	1	23	2,300
					65	98	9,800
4-bromoacetophenone	butylacrylate	3(0.2)	NaO_2CCH_3	140[g]	2	32	160
4-bromoacetophenone	butylacrylate	5(0.2)	NaO_2CCH_3	140	1	53	265
					20	100	500
4-bromoacetophenone	butylacrylate	4(0.2)	NaO_2CCH_3	140	1	10	50
					13	100	500

[a]Reaction conditions: 50 mmol aryl bromide, 70 mmol alkene, 55 mmol base, 30 ml dimethylacetamide. [b]Determined by GC and/or ^{1}H NMR of reaction mixture samples, based on aryl bromide. [c]Refers to temperature of the heating bath, internal temperature range ~ 160-165 °C. [d]100 mmol. [e]Substantial polystyrene formation observed. [f]With 5 equivalents of tris(2,4-di-*tert*-butylphenyl)phosphite. [g]Under air

As with reactions catalysed by **1**,[5] the rate of coupling between arylbromides and butylacrylate catalysed by **3** was found to be dependent on the nature of the arylbromide - decreasing substantially with increasing electron density on the aryl ring. Slightly higher rates of activity and ultimate conversions were obtained with 4-bromoanisole as substrate when potassium carbonate was used as the base.

Substantial palladium deposition is seen in the coupling reactions of deactivated bromides at 0.2mol% catalyst concentration. This does not seem to be due to thermal decomposition as **3** shows good thermal stability in dimethylacetamide at 140°C even after 24 hours. Therefore it seems likely that the deposition is due to one or more catalyst deactivation pathways. We have previously demonstrated that addition of excess triarylphosphite to this catalyst system stabilises it against palladium deposition[4] and find here that a substantial increase in activity is observed in the 4-bromoanisole coupling reaction when excess ligand is added.

The high catalytic activity of **2** with its orthometallated aryl group and two phosphino residues[6] prompted us to investigate the use of the notionally similar **4**, the triphenylphosphine adduct of **3**, in the coupling of 4-bromoacetophenone with butylacrylate. However, this catalyst proved to be considerably less active than **3**. The metallated amine complex **5** proved to be at least as effective a catalyst as **3** at 0.2 mol% loading in the coupling of 4-bromoacetophenone with butylacrylate, despite the fact that quite considerable palladium deposition was observed. For this reason we have not currently studied the use of this catalyst further.

In summary, the extremely high catalytic activity and remarkable air and thermal stability of **3**, coupled with the very low cost of the commercially available ligand tris(2,4-di-*tert*-butylphenyl)phosphite - at least two orders of magnitude cheaper than the commonly used ligand tris(2-methylphenyl)phosphine - bodes well for its use not only in Heck reactions but also in other related C-C and C-X coupling processes, which we are currently investigating.

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