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New approaches to high-activity transition-metal catalysts for carbon–carbon bond forming reactions. Rhenium-containing phosphorus donor ligands for palladium-catalyzed Suzuki cross-couplings

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Received (in Cambridge, UK) 11th February 2002, Accepted 3rd March 2002
First published as an Advance Article on the web 18th April 2002

The rhenium complexes (η^5-C_5H_5)Re(NO)(PPh_3)-($(CH_2)_nPR_2$:) (n/R = 0/Ph, 0/t-Bu, 0/Me, 1/Ph, 1/t-Bu), which contain electron-rich and sterically congested phosphido moieties, give active catalysts for the title reaction; typical conditions (toluene, 60–100 °C): aryl bromide (1.0 equiv.), $PhB(OH)_2$ (1.5 equiv.), K_3PO_4 (2.0 equiv.), $Pd(OAc)_2$ (1 mol%), and a $Re(CH_2)_nPR_2$: species or a 1 : 2 $[Re(CH_2)_nPR_2H]^+X^-$/t-BuOK mixture (4 mol% rhenium).

Phosphine adducts of transition metals catalyze an extensive variety of useful carbon–carbon bond forming reactions.[1,2] Over the past five years, the activities of many such systems have been improved by substituting phosphines that are bulkier and/or more electron-rich.[3] Despite these advances, there remains a distinct need for even more active and long-lived catalysts, as well as improvements in selectivities.[4] Although many clever design and high-throughput screening strategies are being assayed,[3,5] the next generation of breakthroughs may require new paradigms far removed from past approaches.

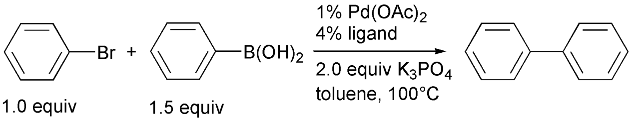
Accordingly, we have sought to develop new catalysts from monodentate phosphorus donor ligands featuring a novel, untested design element: an 18-valence-electron transition-metal center α or β to the phosphorus atom, which would not directly participate in bond breaking/making steps of the catalytic cycle. Such coordinatively saturated L_nMPR_2: and $L_nMCH_2PR_2$: species have an extensive literature. They, and/or nitrogen or sulfur analogs,[6–9] have been shown to be much more basic and nucleophilic than model compounds without the metal, and the underlying reasons have been analyzed in detail.[6,8] A potential concern is that the 'spectator' metal fragment might somehow compromise catalyst lifetimes or stabilities. However, metal-containing ligands of all types[10,11] – not just the familiar ferrocenes[12] – are playing rapidly increasing roles in catalysis. Hence, we set out to probe whether effective catalysts can be generated from rhenium-containing phosphido species, with L_nM equal to (η^5-C_5H_5)Re(NO)(PPh_3). Chelating diphosphines derived from this chiral template give long-lived rhodium hydrogenation catalysts.[11,13]

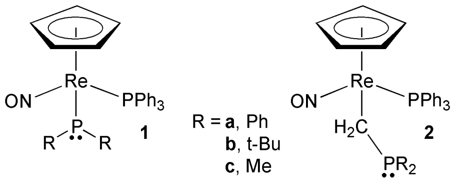
The racemic complexes (η^5-C_5H_5)Re(NO)(PPh_3)(PR_2) (**1**; R = Ph, **a**; t-Bu, **b**; Me, **c**) and (η^5-C_5H_5)Re(NO)(PPh_3)(CH_2PR_2) (**2a**,**b**) shown in Table 1 were isolated *via* deprotonations of the corresponding phosphonium salts $[(\eta^5$-$C_5H_5)Re(NO)(PPh_3)((CH_2)_nPR_2H)]^+X^-$ (n/R = 0/Ph, **3a**$^+$TfO$^-$; 0/t-Bu, **3b**$^+$TfO$^-$; 0/Me, **3c**$^+BF_4^-$; 1/Ph, **4a**$^+PF_6^-$; 1/t-Bu, **4b**$^+BF_4^-$) with t-BuOK, as previously described in most cases.[6,7,11,14] New candidates for high-activity phosphine ligands are often evaluated in palladium-catalyzed Suzuki cross-couplings of aryl bromides and aryl boronic acids.[2,5] Indeed, **1**–**2** gave effective catalysts. However, such species are easily oxidized to phosphine oxides.[6] For convenience, subsequent experiments utilized **1**–**2** that had been generated *in situ* from t-BuOK (2.0 equiv.) and the phosphonium salts, which have shelf-lives of years. The similar use of protonated organophosphines in several palladium-catalyzed reactions was recently reported.[15]

The coupling of phenyl bromide and phenylboronic acid was studied at 100 °C as indicated in Table 1, with K_3PO_4 as the boron-activating base and $Pd(OAc)_2$ as the palladium source.[16] Phenyl bromide disappeared as depicted in Fig. 1, and biphenyl appeared at a similar rate. On the time scale of 0.5–1.0 h, the catalysts derived from ligands **1a**,**b** were distinctly more reactive than those derived from **1c** (less bulky) and **2a**,**b** (less bulky and electron-rich). The *tert*-butyl-substituted ligand **1b** gave the most active catalyst, and this rate was also monitored at 80 and 60 °C to improve time resolution. It was generally close to that of the catalyst from the related organophosphine P(t-Bu)$_3$,[15b] which is one of the best for Suzuki couplings [conversions, **1b**/P(t-Bu)$_3$: 80 °C, 84%/88% (0.25 h), 99%/96% (0.5 h); 60 °C, 21%/79% (0.25 h), 74%/86% (0.5 h)].[3b] The phenyl-substituted ligand **1a** gave a somewhat less active catalyst than PPh_3. Curiously, the catalyst derived from **2b** was less reactive than unmodified $Pd(OAc)_2$. As a possible contributing factor, we speculate that $ReCH_2PR_2PdX$ systems might equilibrate with reactive $^+Re{=}CH_2$ and $[R_2PPdX]^-$ species. However, ^{31}P NMR spectra of **1b**/$Pd(OAc)_2$ mixtures showed only pairs of coupled signals, consistent with intact Ph_3PReP(t-Bu)$_2$ linkages. The initial rate with **1c** was also low, but high yields were achieved with long reaction times (Table 1).

The two best rhenium-containing ligands, **1a**,**b**, were applied to other Suzuki reactions. As summarized in Table 2, > 99–78% yields of the corresponding biaryls were obtained. All reactions with **1b** were complete in < 1 h at 100 °C. Entry 8 in Table 2 was repeated, but on a five-fold greater scale. Chromatography gave the biaryl product in 97% yield. Entries 7 and 8 were repeated, but with reduced palladium and rhenium loadings (0.1 and 0.4 mol%). After 1.0 and 0.5 h, quantitative aryl bromide

Table 1 Survey of Suzuki coupling conditions





Entry[a]	Ligand[b]	Conversion (BrPh/%)[c]	Yield (PhPh/%)[c]	Time/h
1	**1a**	100	93	2
2	**1b**	100	97	0.5
3	**1c**	100	96	96
4	**2a**	100	90	24
5	**2b**	76	57	168
6	PPh_3	100	95	1
7	P(t-Bu)$_3$	100	97	0.5
8	No ligand	66	59	168

[a] Reaction scale: 0.448 mmol of bromobenzene. [b] The ligands in entries 1–5, 7 were generated *in situ* from protonated precursors as described in the text. [c] Determined by GC, *vs.* tridecane as internal standard.

DOI: 10.1039/b201512a

conversions and biaryl yields were again obtained, establishing that turnover numbers of $\geqslant$1000 can be realized.

Ligand **1b** also effected Suzuki couplings of chlorobenzene, but not as rapidly as P(t-Bu)$_3$ (conversions, 100 °C: 40%/168 h *vs.* 83%/96 h). Since K_3PO_4 is only moderately less basic than the t-BuOK used to deprotonate the $[Re(CH_2)_nPR_2H]^+X^-$ ligand precursors [$\Delta pK_a(H_2O)$ *ca.* 6],[17] we wondered whether the latter was needed at all. Accordingly, when a toluene solution of **3b**$^+$TfO$^-$ was treated with K_3PO_4 (2.0 equiv) at 100 °C, the characteristic orange-red color of **1b** was generated. Entry 2 of Table 1 was repeated with this sample. After 0.5 h, the conversion and yield were 100 and 99%. An identical reaction was conducted, but with all components mixed simultaneously. The rate and yield data were essentially identical.

The above data clearly establish the viability of transition-metal-containing monodentate phosphorus donor ligands such as **1** and **2** for palladium-catalyzed Suzuki reactions. The most bulky and electron-rich ligand (**1b**) often comes close to the activity of the corresponding organophosphine. Although the other ligands are less effective, we consider these to be highly promising lead results, amenable to further optimization and extendable to other metal fragments as well as related carbon–carbon bond forming reactions. Furthermore, **1** and **2** are easily obtained in enantiomerically pure form.[6,11] Hence, applications to enantioselective catalysis can be anticipated.[18] The utilization of **1** and **2** in additional types of transition-metal-catalyzed reactions will be reported in the near future.

We thank the Deutsche Forschungsgemeinschaft (GL 300/4-1), the von Humboldt Foundation (fellowship to O. D.), and Johnson Matthey PMC (palladium loan) for support.

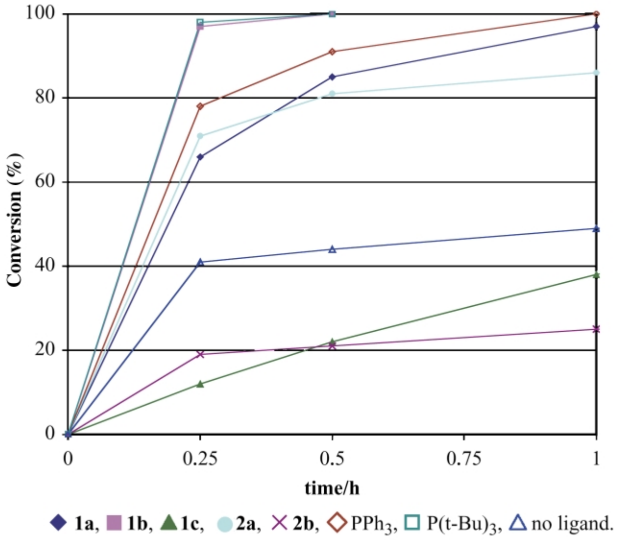
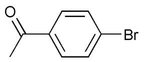
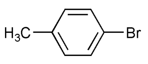
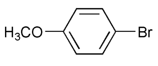
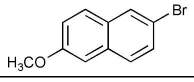


Fig. 1 Rate of consumption of phenyl bromide under the conditions of Table 1.

Table 2 Survey of aryl bromides

$$\text{ArBr} + \text{PhB(OH)}_2 \xrightarrow{\text{See Table 1}} \text{ArPh}$$

Entry	ArBr	Ligand	Conversion (ArBr/%)	Yield (ArPh%)	Time/h
1		**1a**	100	86	0.25
2		**1b**	100	78	0.25
3		**1a**	100	100	4
4		**1b**	100	100	1
5		**1a**	100	88	4
6		**1b**	100	88	0.25
7		**1a**	100	100	0.25
8		**1b**	100	100	0.5

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14 Complexes **1c**, **2b**, **3c**$^+$BF$_4^-$, and **4b**$^+$BF$_4^-$ have not been reported earlier, but all preparative and spectroscopic details are analogous to the other compounds.

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16 *General procedure*: an oven-dried Schlenk flask was charged with the phosphonium salt or phosphine (0.0179 mmol, 4.0 mol%) and dry toluene (4 mL). A 1.0 M THF solution of t-BuOK (0.036 mL, 0.036 mmol) was added with stirring (for phosphonium salts only; rhenium systems turn from yellow to orange-red). After 5 min, a 0.0045 M toluene solution of Pd(OAc)$_2$ (1.0 mL, 0.0045 mmol, 1 mol%), phenylboronic acid (0.082 g, 0.67 mmol, 1.5 equiv.), K_3PO_4 (0.190 g, 0.897 mmol, 2.0 equiv.), an internal standard [0.204–0.205 mmol of tridecane (0.050 mL), hexadecane (0.060 mL), or eicosane (0.058 g)], and the aryl halide (0.448 mmol, 1.0 equiv.) were added. The suspension was stirred (80 or 100 °C) and monitored by GC. The product was identified by comparison of its GC retention time to that of a commercial sample.

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