Cross-Coupling Reactions

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An Efficient Bimetallic Rhodium Catalyst for the Direct Arylation of Unactivated Arenes**

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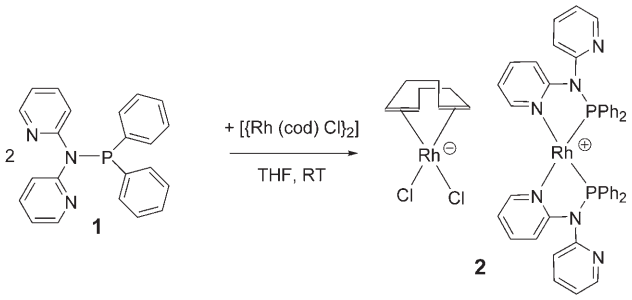
The synthesis of polynuclear coordination compounds and especially of systems with different metal atoms or the same metal atoms in different chemical environments is intensively investigated.[1] Motivation for this interest results from possible applications in homogeneous catalysis because many highly efficient biocatalysts[2] and heterogeneous catalysts[3] are multimetal systems.[4] Despite considerable progress concerning the coordination chemistry of polynuclear compounds there are not many molecular bimetallic catalysts which show a different substrate activation to the single (separated) metal components.[5] Biaryls are an important class of compounds that are accessible through a large variety of metal-catalyzed cross-coupling reactions. Usually arylated organoelement reagents (boron (Suzuki),[6] magnesium (Kumada),[7] silicon (Hiyama),[8] tin (Stille),[9] or zinc (Negishi)[10]) and aryl halides are coupled, in palladium- or nickel-catalyzed reactions. An attractive alternative is a direct arylation which involves a C–H bond functionalization.[11,12] A prerequisite for an efficient reaction is a directing group. The arylation of unactivated arenes, for example benzene, which do not have a directing group, remains challenging.[13,14] Fujita, Yamaguchi, and Nonogawa, for instance, were able to couple aryl iodides in reactions with relatively high catalyst loadings (5 to 10 mol%) and turnover numbers (TONs) up to 15[13] and Fagnou and Lafrance describe a palladium-catalyzed arylation of benzene with aryl bromides in the presence of pivalic acid.[14] We introduced a P,N-ligand system[15] and report herein on a novel bimetallic rhodium complex which is stabilized by such ligands and efficiently catalyzes the nondirected direct arylation.[13,14] In addition to aryl iodides, aryl bromides and chlorides can be cross-coupled. The bimetallic assembly is necessary for catalysis because the two separated single components are catalytically inactive.

The reaction of [bis(2-pyridyl)amino]diphenylphosphane (**1**, PN) with half an equivalent of $[\{Rh(cod)Cl\}_2]$ (cod = 1,5-cyclooctadiene) leads to **2** (Scheme 1). The NMR spectroscopic data of **2** are in accordance with the results of an X-ray crystal-structure analysis (Figure 1).[16] Compound **2** is a bimetallic complex—a saltlike compound—which consists of a $[Rh(cod)Cl_2]^-$ ion[17] and a P,N-ligand-stabilized cation $[(PN)_2Rh]^+$. One of the two pyridyl moieties of the P,N-ligands does not coordinate to the metal center and in solution an exchange of the coordinated and the noncoordinated pyridyl moiety is detected, this exchange requires a rotation around the P–N bond. About 24 rotations per second take place at room temperature (NMR spectroscopic experiments).



Scheme 1. Synthesis of **2**. After washing with hexane, the product was isolated in 98% yield.

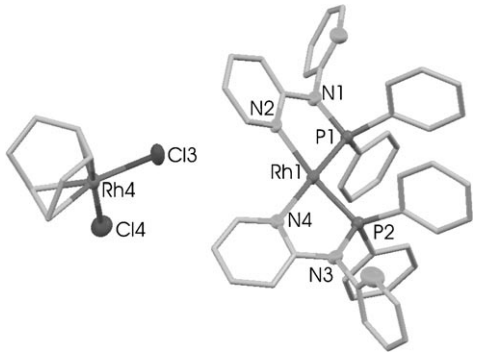


Figure 1. Molecular structure of **2** (H atoms omitted). Selected bond lengths [Å] and angles [°]: P1–Rh1 2.1761(15), P2–Rh1 2.1729(14), N4–Rh1 2.130(4), N2–Rh1 2.143(4), Cl3–Rh4 2.3758(15), Cl4–Rh4 2.3679(12); N4-Rh1-N2 101.12(16), N4-Rh1-P2 81.76(12), P2-Rh1-P1 97.65(6), N2-Rh1-P1 81.67(12).

For the nondirected direct arylation of benzene with aryl iodides compound **2** is a more efficient catalyst than the catalysts described to date. Benzene is arylated by iodobenzene with a TON of 780 in a shorter period of time and under milder conditions than the current best catalyst ($[\{Cp^*Ir(H)Cl\}_2]$, TON = 14; $Cp^* = C_5Me_5$; Table 1).[13] An increased efficiency is observed for other substrates as well. The reaction of $[Rh(cod)_2][B(Ar_F)_4]$ with two equivalents of **1** leads to $[(PN)_2Rh][B(Ar_F)_4]$ (**3**; $Ar_F = C_6H_3(CF_3)_2$). Replac-

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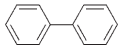
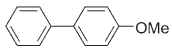
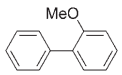
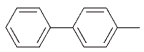
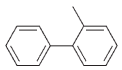
Table 1: Turnover numbers (TONs) for the nondirected direct arylation of benzene by aryl iodides.

Product	**2**[a,b]	**3**[a,b]	**4**[b]	[{Cp*Ir(H)Cl}$_2$][c,d]
	780	0	0	14
	45	0	0	13
	30	0	0	3
	40	0	0	11
	32	0	0	4
	13	0	0	2

[a] Generated in situ from the corresponding rhodium–COD complexes and **1**.[19] [b] 70 °C, 24 h. [c] Cp* = pentamethylcyclopentadienyl. [d] 80 °C, 30 h; values from ref. [13].

ing the anion in **2** (use of **3**) or the cation (use of [NEt$_4$][Rh(cod)Cl$_2$] (**4**))[18] by a rhodium-free counterion results in no catalytic activity (Table 1). Thus, the bimetallic nature of **2** plays an important role in terms of the observed catalytic efficiency.

Furthermore, we were interested in the question: can aryl bromides and chlorides be activated by **2** as well and do they undergo catalytic direct arylation as observed for iodides? Compound **2** activates chlorobenzene in a (pseudo) first-order reaction (Figure 2). The reaction order in chlorobenzene, determined by the isolation method, is 0.99 ± 0.01. The temperature dependence of the rate constants of the activation reaction gave rise to the following activation parameters: $\Delta H^{\neq} = (41.5 \pm 0.7)\ \mathrm{kJ\,mol^{-1}}$, $\Delta S^{\neq} = (-171 \pm 2)\ \mathrm{J\,K^{-}\,mol^{-}}$. Activation parameters for the activation of C–Cl bonds by

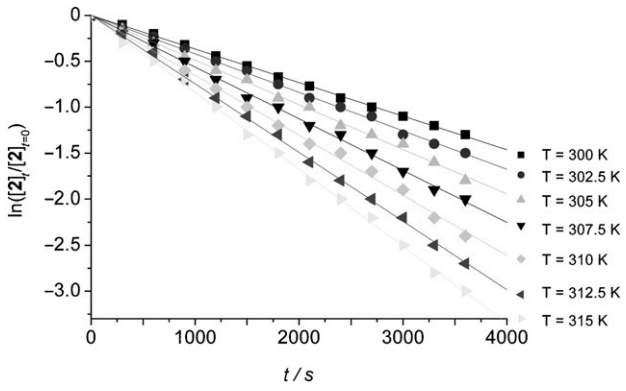
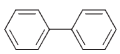
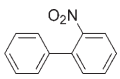
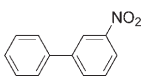
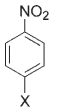
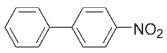
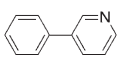


Figure 2. (Pseudo-)first-order kinetics for the reaction of **2** and chlorobenzene (excess) at different temperatures ([**2**]$_t$: concentration of **2** at time *t*).

Group 9 metal complexes are rare. For comparison, a drastically higher activation enthalpy ($E_a = 64\ \mathrm{kJ\,mol^{-1}}$) was observed for the activation of CH_3Cl at $[Ir(CO)_2Cl_2]^-$ ions.[20] In agreement with the relatively efficient stoichiometric activation of chlorobenzene, **2** is able to couple aryl bromides and chlorides catalytically (Table 2). The intermolecular

Table 2: Nondirected direct arylation of benzene by aryl bromides and chlorides.[a]

Aryl halide	Product	Yield [%] X = Br[b]	Yield [%] X = Cl[c]
		65	46
		96	73
		87	61
		83	70
		83	59

[a] 70 °C, 24 h. Compound **2** was generated in situ from [{Rh(cod)Cl}$_2$] and **1**.[19] [b] 5 mol% **2**. [c] 10 mol% **2**.

directed direct arylation using aryl chlorides has hardly been described. An efficient ruthenium-based catalyst system was recently introduced by Ackermann and coworkers.[12t,u] The direct arylation of aryl bromides and chlorides catalyzed by **2** tolerates functional groups, such as nitro groups (Table 2), whereas the catalyst system based on [{Cp*Ir(H)Cl}$_2$] does not. For example, no conversion was observed for the coupling of 4-iodonitrobenzene with benzene.[13] From the selectivity data for the arylation of toluene with [{Cp*Ir(H)Cl}$_2$] it was concluded that the reaction proceeded via radical intermediates.[13] The same conclusions can be dawn from the corresponding data for the nondirected arylation using our catalyst system. Arylation of toluene (iodobenzene) catalyzed by **2** leads to 71% *ortho*-, 19% *meta*-, and 10% *para*-phenyltoluene. The results of a Hammett correlation (Figure 3) are also in accordance with radical pathways. For the catalyst system **2**, a slope of $\rho = 1.33 \pm 0.02$ (Figure 3) is found indicating the participation of radical intermediates.[22]

For future work we are interested in the development of the catalyst system, for instance, by P,N-ligand variation, in addressing the selectivity issue, and in sequential activation and functionalization of unactivated aromatic C–H bonds. As the investigated substrate range indicates, a directing group can easily be introduced by nondirected C–H activation and

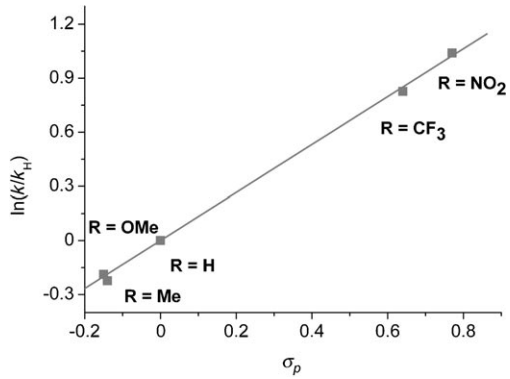


Figure 3. Hammett correlation of the direct arylation of benzene, with $\ln(k/k_H) = \sigma_p\rho$ and $\rho = 1.33 \pm 0.02$ (k/k_H: reduced rate constant, σ_p: Hammett substitution constant (*para* substitution)).[21]

subsequently gives access to highly functionalized molecules by a further selective, directed, C–H activation reaction.

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[16] *R* values: $R_1 = 0.040$, $wR_2 = 0.074$ ($I > 2\sigma(I)$); $R1 = 0.093$, $wR2 = 0.085$ (all data). CCDC-626623 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
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[19] The following THF stock solutions (**SL**) were prepared: [{Rh(cod)Cl}$_2$]: 0.005 M (**SL1a**), 0.05 M (**SL1b**), 0.25 M (**SL1c**), and 0.5 M (**SL1d**); [Rh(cod)$_2$][B(Ar$_F$)$_4$]: 0.005 M (**SL2a**) and 0.05 M (**SL2b**); [NEt$_4$][RhCl$_2$(cod)]: 0.00125 M (**SL3a**) and 0.0125 M (**SL3b**); ligand **1**: 0.01 M (**SL4a**), 0.1 M (**SL4b**), 0.5 M (**SL4c**), and 1 M (**SL4d**). All aryl halides were dissolved to give a 1 M THF solution. A pressure tube was filled with KO*t*Bu (339 mg, 3.3 mmol), with **SL1** or **SL2** (0.2 mL), and with the corresponding **SL4,** or with **SL3** (0.4 mL). The aryl halide solution (1 mL) and benzene (0.89 mL, 0.78 g, 10 mmol) were then added. The mixture was stirred at 70 °C for 24 h. Yield was determined by GC.

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