Homogeneous and heterogenized Au(III) Schiff base-complexes as selective and general catalysts for self-coupling of aryl boronic acids†

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A series of homogeneous and heterogenized gold metal complexes show high activity and selectivity for the homocoupling of a large variety of aryl boronic acids, being of general utility for the synthesis of C_2-symmetric biaryls.

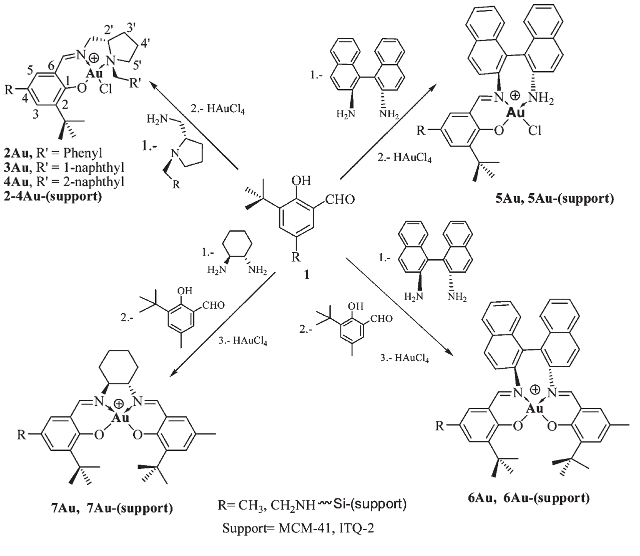
Coupling of aryl boronic acids and esters with organic halides is an excellent method for preparing symmetrical and unsymmetrical biaryls, which are important building blocks in natural products and in materials sciences.[1] Biaryls exhibit a wide variety of physical and chemical properties[2] with versatile applications in pharmaceuticals, polymers, nonlinear optics,[3] liquid crystals,[4] and optically active ligands.[5] The diverse applications of these molecules have recently led to a number of transition metal catalyzed approaches to yield the biaryl moiety. Suzuki coupling has become increasingly popular due to its compatibility with a variety of functional groups, the stability of the organoboron precursors, and the ease of working up the reaction mixture. As such, a wide variety of aryl boronic acids are available commercially. Self-coupling of aryl groups of the aryl boronic acids is very slow.[6] We have observed that selective formation of self-coupling products occur under Suzuki-catalyzed reaction conditions when using gold(III), and therefore our attention has been directed towards the application of the self-coupling reaction as a synthetic method for allowing a wide variety of C_2-symmetric biaryls.[7] Selective homocoupling with halogenated aryl boronic acids represents a new way for the synthesis of halide biaryls difficult to prepare by typical Pd-Suzuki catalyzed reaction.

Herein we present a very easy and widely applicable approach using Au(III)-complexes and supported Au(III)-complexes on silica based mesoporous and laminar inorganic solids for the homocoupling of aryl boronic acids.

Metal complexes were prepared under dinitrogen by conventional Schlenk-tube techniques, and solvents were carefully degassed before use. Then, in the case of gold complexes, an ethanolic solution of anhydrous $HAuCl_4$ (97 mg, 0.27 mmol) was added to a solution of the ligand in EtOH (30 ml) at room temperature. The resultant mixture was stirred under reflux for 10 h, cooled to room temperature and then concentrated under vacuum. The residue was washed several times with diethyl ether, dried and filtered to afford the respective complexes in almost quantitative yields. Complexes are characterized by their analytical and spectroscopic data, their stoichiometry is confirmed by ESI-mass spectrometry that shows ion molecular peaks.†

The preparation of immobilized ligands and complexes involves the anchoring of precursors bearing triethoxysilyl groups onto pure mesoporous silica[8] and on a delaminated zeolitic material (ITQ-2), as shown in Scheme 1.

The organically modified[8] silica based supports, *i.e.*, MCM-41[9] and delaminated zeolitic materials,[10] were prepared in the following way: A solution of 2 mmol of 5-azidomethyl-3-*tert*-butyl-2-hydroxybenzaldehyde in toluene (5 ml) was added to a suspension of the siliceous support (2 g) in toluene (25 ml), and stirred at room temperature for 30 min. The slurry was heated at 100 °C for 16 h and the yellow solid was filtered off and washed successively with toluene, petroleum ether, ethanol and ether. Then, 1 mmol of the anchored hydroxyaldehyde **2**–(Sil, MCM-41, ITQ-2) was suspended in ethanol (10 ml) under Ar at room temperature. After 10 min, 125 mg (1.1 mmol) of the amine were added and stirred for 16 h. The deep yellow solid was filtered and washed thoroughly with ethanol and then with ether. The solid was dried under vacuum to afford the corresponding anchored ligands [ligand–(support)]. The heterogenized complexes were synthesized as follows. An ethanolic solution of $HAuCl_4$ (0.5 mmol, 15 ml) was added to a toluene (20 ml) suspension of heterogenized ligand at room temperature. The resulting mixture was stirred under reflux for 12 h, cooled to room temperature and filtered. The solid was washed several times with ethanol, dried and filtered to afford the respective heterogenized complexes, complex–(support), in almost quantitative yields. Supported complexes are characterized by their spectroscopic and analytical



Scheme 1 Synthesis of soluble and heterogenized Au-complexes.

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† Electronic supplementary information (ESI) available: experimental data, analytic and spectroscopic methods and results. See http://www.rsc.org/suppdata/cc/b4/b418897g/
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data, ICP-analysis showed a metal content of 0.30–0.60 mmol g^{-1}; these values were used in catalytic experiments.† In the IR spectroscopic characterization, the peaks due to the support dominate the spectra of the heterogenized catalyst. Nevertheless, some of the bands characteristic of the complexes could be distinguished. The 1600 cm^{-1} band can be assigned to C=C and azomethine C=N vibrations, shifted to lower wavenumbers (relative to the free ligands) due to N^{-} coordination of the imine. Bands in the 500–600 cm^{-1} region are present and ascribed to δ(M–O).

The DFTR spectra for all complexes were obtained in the 200–800 nm range. The complexes show several band maxima in the UV region which agree with the assignment of the bands as intraligand $\pi \rightarrow \pi^*$, $n \rightarrow \pi^*$ transitions in the aromatic ring, azomethine group and charge-transfer transitions. The bands in the 400–500 nm region correspond to d–d transitions expected for planar complexes[11] and MLCT bands. The diffuse reflectance spectra of M–(ligand) complexes are almost identical before and after heterogenization, indicating that the complexes maintain their geometry and electronic characteristics after heterogeneization without significant distortion.

Diamagnetic gold complexes have also been characterized by ^{13}C NMR spectroscopy. In all cases, the spectra show the simultaneous occurrence of two sets of signals which can be related on one hand to the substituted benzaldimine entity, and on the other hand to the aliphatic part of the ligand. The ^{13}C NMR spectra showed the signals assigned to C=N carbon highfield shifted and C$_1$ at $\delta \sim 162$ ppm downfield shifted confirming that metallation has occurred.

The FTIR, DFTR and ^{13}C NMR spectra for complex **7Au**–MCM-41 are given as an example in supplementary material.

The soluble gold complexes and complexes bound on MCM-41 and delaminated zeolites have been tested in the homocoupling reaction between aryl boronic acids, using *o*-xylene as solvent. All prepared catalysts give high yields of the homocoupling reaction with TON 53.3–66.0 mol converted per mol gold. The results for complex **7Au** and its corresponding heterogenized **7Au**–(MCM-41) are given, as an example, in Table 1.

The effect of electron donating and electron withdrawing substituents on conversion and yields was studied, and it can be concluded that, in general, electron withdrawing or electron donating substituents did not significantly change the yield of the substituted biphenyl. Furthermore, no significant steric effect was exhibited for the aryl boronic acids tested.

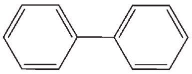
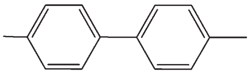
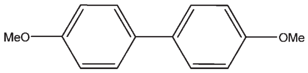
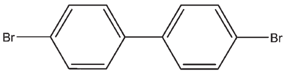
In an additional experiment phenyl boronic acid was reacted with 4-bromophenyl boronic acid under the same conditions than above, and the results showed a ratio (1 : 1 : 0.5) for phenyl–phenyl, 4-bromophenyl–4-bromophenyl and phenyl–4-bromophenyl products respectively indicating that the homocoupling products were obtained in the same ratio (1 : 1) and the aryl boronic cross-coupling product is obtained as a minor product.

We have also examined the prepared **7Au** complexes (homogeneous and heterogenized) catalyzed reaction for the typical Suzuki conditions between BrPh and *p*-BrPhB(OH)$_2$, and the expected cross-coupling product was not formed while the aryl boronic homocoupling compound was obtained as the exclusive product (Table 2). The same results, *i.e.*, 100% selectivity towards the homocoupling product were obtained when the reaction was carried out in air. We have investigated the general utility of the catalyst and reaction conditions with a variety of aryl boronic acid substrates (aryl = phenyl, 4-BrPh, 4-OMePh, 4-MePh) and aryl halides (BrPh, IPh, 1-bromonaphthalene, 1-bromo-4-methoxybenzene) and we have obtained 100% homocoupling selectivity for all tested reactions.

It has to be remarked that when the corresponding homogeneous palladium catalysts bound on MCM-41 and delaminated zeolites have been tested for the same Suzuki reactions, under the same reaction conditions, the results (Table 2) show that

Table 1 **7Au** and **7Au**–(MCM-41)-catalyzed homocoupling of selected reaction partners[a]

$$\text{Ar-B(OH)}_2 \xrightarrow[\text{K}_2\text{CO}_3\text{, Xylene}]{\text{Au catalyst}} \text{Ar-Ar}$$

	Yield (%)[b]					
Product	**7Au**	**7Au**–(MCM-41)	**6Au**	**6Au**–(MCM-41)	**2Au**	**2Au**–(MCM-41)
	93	97	97	99	95	96
	85	96	97	97	92	92
	81	94	96	97	92	92
	80	94	95	95	90	91

[a] Conditions: aryl boronic acid (10 mmol.), gold catalyst (0.3 equiv.), and K$_2$CO$_3$ (20 mmol) in xylene at 130 °C. [b] Yields were determined from isolated samples of the reaction after 24 h.

Table 2 Summary for all prepared Au(III)- and Pd(II)-complex catalyzed cross-coupling at Suzuki's reaction conditions[a]

$$\text{Ar - X} + \text{Ar}'\text{-B(OH)}_2 \xrightarrow[\text{Xylene}]{\text{Au, Pd}} \underset{\textbf{A}}{\text{Ar}'\text{-Ar}'} + \underset{\textbf{B}}{\text{Ar-Ar}} + \underset{\textbf{C}}{\text{Ar}'\text{-OH}}$$

			Au[b]			Pd[b]		
Ar	X	Ar′	A(%)	B(%)	C(%)	A(%)	B(%)	C(%)
Ph	Br	Ph	90–92	0	3–5	0	85–90	traces
Ph	I	Ph	>90	0	0	0	65–70	0
4-OMePh	Br	Ph	95–99	0	traces	5–10	40–50	0
Naphth	Br	Ph	91–98	5–10	0	2–5	45–50	5–8
Ph	Br	4-MePh	91–95	0	traces	0	50–60	traces
Ph	I	4-MePh	>90	0	0	0	40–50	traces
Ph	Br	4-OMePh	90–95	0	traces	0	50–60	0
Ph	Br	4-BrPh	90–93	0	traces	20	60–65	0

[a] Conditions: aryl boronic acid (10 mmol.), aryl halide (15 mmol), Au or Pd catalyst (0.3 equiv.), and K_2CO_3 (20 mmol) in xylene at 130 °C. Yields were determined, for various catalysts, by GC analysis of the crude reaction mixtures at 24 h. [b] Range of yields for all catalysts in each reaction.

Pd-catalysts are highly selective towards cross-coupling reactions, and only when the reaction was very slow, some homocoupling reaction between boronic acids also occurred. It is worth mentioning that under the same reaction conditions and with the same amount of gold but in the form of $AuHCl_4$ only 12% yield for homocoupling was observed after 24 h. At present we can only speculate on the mechanistic differences between Au and Pd catalysts. Nevertheless, it is well accepted[12,13] that Suzuki cross-coupling involves an oxidative addition of phenyl halide to the Pd as the first step. Since the Au complex is unable to perform the cross-coupling, but produces the homocoupling instead, we may assume in a first approximation that the oxidative addition does not occur on gold and the homocoupling may occur through an "aromatic transmetallation" from the boron to the gold; in a second transmetallation the gold complex will bind a second aromatic ring which finally will give biphenyl by reductive elimination while regenerating the original Au complex through ligand rearrangement In Scheme 2 we have included this tentative mechanism.

In summary we have obtained selectively a gold-catalyzed aryl boronic acid homocoupling reaction using a protocol similar to the well documented cross-coupling reaction. The general conditions used here are applicable to a variety of substituted boronic acids. This method has a number of advantages including the mild reaction conditions, easily isolable products, and characteristic yields associated with the homocoupling *versus* cross-coupling reaction.

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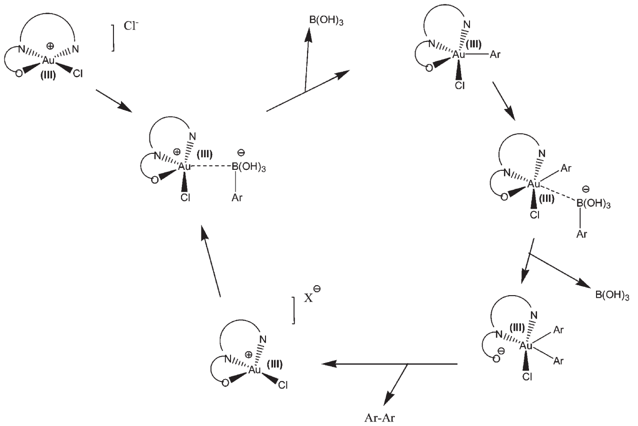

Scheme 2 Tentative mechanism for self-coupling of aryl boronic acids with Au complex.

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