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Efficient catalysis of Ullmann-type arylation reactions by a novel trinuclear copper(I) complex with a chelating tricarbene ligand

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Abstract

A novel trinuclear copper(I) complex with a chelating tricarbene ligand is shown to be an efficient catalyst for the arylation of different classes of compounds containing N–H or O–H functions. Different kinds of azole rings (pyrazole, imidazole, 1,2,4-triazole) can be arylated with comparable efficiencies at relatively mild temperatures ($100 \,^{\circ}$ C). The catalyst activates aryl iodides, bromides and even chlorides for the reaction. An unusually strong influence of the nature of the aryl substituent on the reaction yield is observed. The synthetic protocol can be extended to other substrate classes, such as phenols and amides, although the catalytic efficiency with amides is significantly reduced. © 2008 Elsevier Ltd. All rights reserved.

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1. Introduction

Palladium-catalyzed carbon-carbon and carbon-heteroatom cross-coupling reactions have become one of the most important reaction classes in chemical synthesis.¹ Some of these reactions, most notably the Heck reaction,² the Suzuki-Miyaura reaction,³ and the C–N coupling of organic halides with nitrogen-containing compounds (the so-called Buchwald-Hartwig coupling)⁴ have been developed to a high degree of synthetic utility. However, since all these reactions need a palladium catalyst (albeit in extremely low amount in some cases⁵), the cost of the metal catalyst may become an issue for their technological application. Therefore, a flourishing area of research is the quest for catalysts made out of non-noble metals, which exhibit comparable catalytic efficiency. Interesting results have been obtained with nickel catalysts,⁶ but in the last few years copper catalysts have undoubtedly taken the lead.⁷

Copper is a very well known catalyst for cross-coupling reactions, since Ullmann and Goldberg discovered at the

beginning of the last century, the reactions later named after them, namely the C–N coupling of aryl halides with amines or amides.^{8,9} The scope of these reactions was later extended to include the coupling of aryl halides with other compounds containing an N–H or O–H function.¹⁰ However, despite extensive research in that area, the classical Ullmann, Goldberg and related reactions were invariably plagued by the need for large amounts of copper (in the form of salts, oxides or finely divided metal) and for very harsh reaction conditions, most notably for a high reaction temperature. Therefore, as palladium complexes much later emerged as extremely versatile catalysts also for many C–N cross-coupling reactions,⁴ research on copper catalysts almost subsided.

More or less at the turn of the century, however, two novel approaches have made it clear that copper-catalyzed crosscoupling reactions can be run under much milder, technologically attractive reaction conditions. On the one hand, it was demonstrated that copper(II) acetate can promote^{7d,11} or even catalyze^{7d,12} the coupling of organometallic reagents, most notably aryl- and vinylboronic acids, with many different compounds containing an N–H or O–H function, at room temperature; simple copper(I) salts were later also found to be active, albeit at higher temperature.¹³ On the other hand, it was also

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shown that simple copper(I) complexes formed in situ with chelating nitrogen- and/or oxygen-containing ligands could effect N- and O-arylations of many different organic compounds with aryl halides in good yields at temperatures in the range 80-150 °C.^{7a-c} This approach has been pioneered by the groups of Buchwald,¹⁴ Ma,¹⁵ Taillefer,¹⁶ as well as others,^{7a-c,17} and it is currently regarded as a more promising synthetic strategy, given the low cost and wide availability of the aryl halide substrates as opposed to the organometallic reagents needed for the previous approach. The range of employed ligands is continuously increasing,^{7a-c,14-17} and other kinds of copper-containing catalysts, such as Cu₂O-coated soluble copper nanoparticles,¹⁸ copper-exchanged apatites,¹⁹ and copper-containing perovskites²⁰ have been successfully tested as well.

We have recently started a research project aimed at the catalytic application of novel transition metal complexes with *N*-heterocyclic carbene (NHC) ligands.²¹ Such complexes have gained considerable reputation as homogeneous catalysts in the course of the last ten years,²² applications ranging from second-generation olefin metathesis²³ to C–C and C–N coupling reactions,²⁴ hydrosilylations,²⁵ telomerizations,²⁶ and selective alcohol oxidations with molecular oxygen.²⁷ Remarkably, the vast majority of these highly successful applications involve monocarbene complexes, i.e., complexes containing only one NHC ligand. There are also several examples



Scheme 1. Cu_6 -octahedral complex (1).

of metal complexes with dicarbene ligands,²⁸ but only very few ones involving tricarbene ligands.^{28–32} In the frame of our research project, we became interested in the tricarbene ligands originally developed by Fehlhammer and co-workers.²⁹ Such ligands are close analogues of the more popular hydridotris(pyrazolyl) borates and proved to be efficient chelating ligands toward first-row transition metal centers such as chromium(III), iron(III) or cobalt(III) as well as toward rhenium-(VII). A Cu₆-octahedral complex (1),³³ in which every Cu atom is coordinated to an imidazolin-2-ylidene moiety of a tricarbene hydrotris(3-methyl-imidazolin-2-ylidene-1-yl)borate unit (Scheme 1) was also reportedly isolated as a byproduct in the reaction of the corresponding dicarbene ligand, dihydrobis(3-methyl-imidazolin-2-ylidene-1-yl)borate, with CuCl to give a dinuclear complex with two bridging dicarbene units.³⁴

Consequently, we set out to evaluate the coordination chemistry of this tricarbene ligand by direct reaction with copper complexes, in the hope of developing a novel well-defined catalyst for cross-coupling reactions.

2. Results and discussion

The tricarbene ligand was synthesized following the procedure described in the literature by Fehlhammer et al., i.e., by reaction of 1 equiv of hydrotris(3-methyl-imidazolium-1-yl)borate bis(tetrafluoroborate) with 3 equiv of *n*-BuLi;²⁹ the in situ produced monoanionic tricarbene was then reacted with the complex [CuBr(PPh₃)₃] without prior isolation (Scheme 2). We have obtained in this way in good yield a well-defined product as a white solid, which can be safely handled in air, although a prolonged air and light exposition causes a certain degree of copper(I) oxidation, as indicated by the appearance of a blue/green color in the solid. We have attributed to the product, hereafter named complex (**2**), the structure reported in Scheme 2, that is, a monocationic trinuclear structure of the type [Cu₃(BH{N(H)C=C(H)N(Me)C}₃)₂]⁺, in which every copper atom is coordinated to two imidazolin-2-ylidene



Scheme 2. Synthesis of complex (2).

rings, belonging to two different tricarbene units, each one therefore coordinating in a μ_3 - η^1 : η^1 : η^1 fashion. This attribution is supported by many different experimental observations, which are reported in the following.

First of all, the ¹H NMR spectra of the copper complex supports the proposed structure. The product appears spectroscopically pure, and exhibits signals slightly upfield in comparison with the parent tris-azolium salt; as expected, the C₂-H signal is absent. Correspondingly, the ¹³C NMR spectrum shows the characteristic coordinated C₂ signal at δ ca. 176.2 ppm, well downfield from the corresponding signal of the tris-azolium salt (δ ca. 139.9). Furthermore, there is only a single set of signals for the imidazolin-2-ylidene rings in both the ¹H and ¹³C NMR spectra, which indicates a highly symmetric structure.

Although we tried to further purify the product by different means, we were unable to obtain complex (2) in pure form as it turned out to be invariably contaminated by lithium salts. If the presence of inorganic material was taken into account, however, the elemental analysis could be fitted with the

proposed structure (see Section 4); this problem has already been reported for a similar complex of Au(I).³⁴ Moreover, the ESI-MS spectrum of (2) gives a unique ion at m/z 701.4; this confirms that (2) indeed possesses an oligomeric structure, with two tricarbene ligands and three metal centers; further support to this hypothesis is also given by the simulation of the isotopic pattern of the mass ion, which perfectly matches the experimental one (Fig. 1).

We have also run an XPS characterization of the product. In Figure 2 the photoelectronic peak of Cu 2p is reported; the shape and the position of the two components, $2p_{3/2}$ and $2p_{1/2}$ (933.0 and 953.0 eV, respectively), are comparable with those reported in the literature for Cu(0) or Cu(I) species;³⁵ furthermore the absence of the shake-up signals excludes the presence of Cu(II) species. Finally the position of the Auger peak allows to distinguish between Cu(0) and Cu(I), its position being expected around 919.0 eV for metal copper and 916.0 eV for Cu₂O;^{35a} the Auger contribution in our sample (Fig. 2) shows that the copper is present in the oxidation state +I.



Figure 1. ESI-MS spectra of complex (2) and simulation of the isotopic pattern for the fragment $[Cu_3(BH{N(H)C=C(H)N(Me)C}_3)_2]^+$.



Figure 2. XPS spectra of complex (2): XP peak of Cu 2p (left); Auger Cu LMM peak (right).

Unfortunately, complex (2) undergoes slow decomposition in solution leading to formation of copper(II) species, which prevented the growth of crystals suitable for further confirmation of the assumed structure by, e.g., X-ray structure determination. Nevertheless, it should be remarked that similar structures have already been proposed in the literature for copper complexes with trispyrazolylborate ligand (3)³⁶ or tricarbene ligand (4)^{30c} (Scheme 3); in the latter case the proposed structure was also experimentally verified by X-ray structure analysis.



Scheme 3. Examples of copper complexes with tridentate ligands having structure similar to (2).

Complex (2) has been employed as catalyst for the arylation of azoles, amides, and phenols with aryl halides. Initially, we took the N-arylation of pyrazole with 4-iodoacetophenone as a standard test reaction (Scheme 4, X=I) with K_2CO_3 as the base.



Scheme 4. N-Arylation of pyrazole with 4-haloacetophenone.

The amount of copper catalyst (1 mol %, i.e., 3 mol % [Cu]) and the reaction time (24 h) were the same for all experiments and were not further optimized. The reaction temperature (100 °C) was also set constant for all reaction tests, since we wanted to evaluate the catalytic performance of (2) at a comparatively low temperature.

First of all, the optimal reaction solvent was investigated. We were somewhat limited by the poor solubility of (2) in nonpolar aprotic solvents; nevertheless, the results reported in Table 1, entries 1–6 clearly show the superiority of dimethylsulfoxide (DMSO) and *N*,*N*-dimethylformamide (DMF) as reaction solvents for this reaction; other dialkylamide solvents such as *N*,*N*-dimethylacetamide (DMA), or *N*-methylpyrrolidinone (NMP) performed worse than DMF, whereas in acetonitrile and 1,4-dioxane the complex was almost inactive.

We then used DMSO and DMF as reaction solvents to screen for the best base. As can be seen from Table 2, entries 1–6, DMSO gave consistently better results than DMF with all the three bases employed. Furthermore, Cs_2CO_3 emerged as the best base among those tested by us. The superiority of Cs_2CO_3 as the base was more clearly seen in the reaction with the less reactive 4-*bromo*acetophenone in DMSO (Table 2, entries 7–9). By running the reaction in DMSO with cesium

 Table 1

 N-Arylation of pyrazole with 4-haloacetophenone: influence of the solvent

Entry	Х	Solvent	Base	Yield ^a (%)
1	Ι	DMF	K ₂ CO ₃	80
2	Ι	DMA	K_2CO_3	46
3	Ι	DMSO	K_2CO_3	90
4	Ι	NMP	K ₂ CO ₃	56
5	Ι	MeCN ^b	K_2CO_3	1
6	Ι	Dioxane	K_2CO_3	1
7	Cl	DMSO	Cs_2CO_3	44
8	Cl	DMF	Cs_2CO_3	30
9	Cl	$BMIM-BF_4^{c}$	Cs ₂ CO ₃	12

Reaction conditions: see Section 4.

^a Yields determined by ¹H NMR spectroscopy.

^b Reaction temperature 82 °C.

^c BMIM-BF₄=1-butyl-3-methylimidazolium tetrafluoroborate.

Table 2

N-Arylation of pyrazole with 4-haloacetophenone: influence of the base

Entry	Х	Solvent	Base	Yield ^a (%)
1	Ι	DMF	K ₂ CO ₃	80
2	Ι	DMSO	K_2CO_3	90
3	Ι	DMF	Cs_2CO_3	95
4	Ι	DMSO	Cs ₂ CO ₃	93
5	Ι	DMF	K_3PO_4	71
6	Ι	DMSO	K_3PO_4	97
7	Br	DMSO	Cs ₂ CO ₃	73
8	Br	DMSO	K_3PO_4	35
9	Br	DMSO	K ₂ CO ₃	54

Reaction conditions: see Section 4.

^a Yields determined by ¹H NMR spectroscopy.

carbonate as the base it was even possible to activate 4-*chloro*acetophenone (Table 1, entry 7); the reaction gave the desired product in 44% yield.

Thus, complex (2) appears to be able to activate an aryl chloride for the coupling reaction with pyrazole at 100 °C, which is a remarkably low temperature for such a reaction; to the best of our knowledge, the only other catalytic systems, which effect the coupling of aryl chlorides with azoles at comparable temperatures were reported by the group of Choudary¹⁹ and of Liu.^{17f} The reactivity of 4-chloroacetophenone in this reaction was also tested in other solvents, such as DMF and the ionic liquid 1-butyl-3-methylimidazolium tetra-fluoroborate (Table 1, entries 8 and 9); however, DMSO remained the most effective solvent for the reaction.

Finally, in order to rule out the possibility that an uncatalyzed nucleophilic substitution reaction contributes to the reaction outcome,^{17h} we performed the reaction between iodoacetophenone and pyrazole without catalyst. While the conversion of the aryl halide was quantitative, the coupling product was produced in very low yield (Table 3, entry 1); we observed instead the dehalogenation product (acetophenone), the homocoupling product (4,4'-diacetylbiphenyl), and another unidentified product not containing the pyrazole ring.

Having optimized the reaction solvent and the employed base we set out to check the generality of the method by running test reactions with differently substituted aryl halides. The results are reported in Table 3. Table 3 N-Arylation of pyrazole with substituted aryl halides

R	_)x	+	N N H	[Cu] 3 mol% Cs ₂ CO ₃ , DMSO T = 100 °C, 24h	
Entry		Ary	l halide	Azole	Yield ^a (%
	N	Иe			

1		NN-H	<5 ^b
2	Me O	∑N ^{−H}	93
3	Me	K ^N N [−] H	21
4	MeO	NN-H	50
5	Me O Br	N-H	73
6	MeOBr	∑N∽H	16
7	Me	^N N [−] H	44

Reaction conditions: see Section 4.

^a Yields determined by ¹H NMR spectroscopy.

^b Reaction performed without catalyst.

It is very well known that arvl substitution may influence the kinetics of oxidative addition processes involving an aryl halide, such as the one, which according to the currently most widely accepted mechanism activates the aryl halide for the present reaction.^{7a,b} Electron-withdrawing substituents are expected to promote oxidative addition and electron-donating substituents to hinder it. Remarkably, the performance of most copper-based catalysts reported in the literature appears to be only marginally dependent on the substituents on the aryl halide: substrates with the same halide atom usually give comparable yields, with the partial exception of substrates substituted in the ortho position, where steric effects come into play. By contrast with this, the electronic properties of the substituent on the aryl halide were found to play a very important role in determining its reactivity with catalyst (2), both with aryl iodides and bromides.

Moreover, the reactivity trend was apparently not directly related to the electron-withdrawing ability of the substituent (acetyl>methyl>methoxy), since 4-iodotoluene turned out to be the least reactive iodide substrate. Remarkably, 'anomalous' reaction trends with differently substituted aryl bromides or chlorides were very recently reported also for some Pd-catalyzed reactions (aminations, Suzuki couplings), but no rationale was proposed for the observed results.³⁷ We are currently looking for an acceptable explanation of our observations, which could be possibly found in differences in the reaction mechanism due to the polynuclear nature of (**2**). Indeed, it has already been shown that polynuclear copper complexes exhibit peculiar catalytic properties in Ullmann-type reactions.¹⁰

It needs here to be once more remarked that the reported reaction yields were not optimized with respect to the amount of catalyst and the reaction time, which were set constant for all experiments. Optimization of these parameters could result in significantly improved yields and/or shorter reaction times. In order to demonstrate this, we have determined the conversion curve of the reaction between pyrazole and 4-iodoaceto-phenone using 0.1 mol % catalyst. The experimental curve reported in Figure 3 shows that, although the reaction was obviously slower than that with 1 mol %, the catalyst was remarkably stable under the employed reaction conditions and allowed to reach about 80% yield after 48 h.

We continued to evaluate the generality of the method by checking the reactivity of different azoles. The results are reported in Table 4. Quite interestingly, the yields obtained with imidazole were very similar to those obtained with pyrazole, irrespective of the aryl halide used. In the case of 1,2,4-triazole, the reactivity of aryl bromides and chlorides was found to be slightly lower than that with the other azoles, whereas aryl iodides gave comparable or even higher yields.

The reactivity exhibited by imidazole and 1,2,4-triazole with catalyst (**2**) is remarkably high, and it contrasts with the results obtained by the group of Taillefer with copper(I) diamine complexes, for which a clear decrease in reactivity in the order pyrazole>imidazole>1,2,4-triazole was observed.^{16a} Furthermore, the reactivity trend observed with pyrazole and differently substituted aryl halides was fully confirmed also with the other azoles: acetyl-substituted substrates were the most reactive, followed by methoxy- and finally by methyl-substituted substrates.

We then turned our attention to coupling partners other than azoles and took amides into consideration. The results are reported in Table 5. It can be clearly seen that catalyst (2) is less efficient in coupling amides than azoles: yields are consistently lower with activated acetyl-substituted aryl halides and almost no reaction is observed already in the case of 4-iodoanisole. Benzamide appears to be somewhat more reactive than pyrrolidinone, for which iodoacetophenone appears to be the



Figure 3. Conversion curve of the reaction between pyrazole and 4-iodoacetophenone using $0.1 \mod \%$ catalyst (2); for the other reaction conditions, see Table 3.

Table 4

N-Arylation of other azoles with substituted aryl halides

$R - \bigvee X + HN \bigvee N$	[Cu] 3 mol% Cs ₂ CO ₃ , DMSO T = 100 °C, 24h	$R - \sqrt{-N} N - N - V - Y$
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Entry	Aryl halide	Azole	Yield ^a (%)
1	Me O	N ^{//} N ^{-H}	>99
2	Me	N [×] N ^{-H}	20
3	MeO	N [×] N ^{-H}	50
4	Me O Br	N~H	70
5	Me O Cl	N ^{//} N ^{-H}	50
6	Me O	N [∕] N ^{−H} \=N	>99
7	Me	N [∕] N ^{−H} ∖= _N	22
8	MeO	N [∕] N ^{−H} ∖= _N	84
9	Me O Br	N [∕] N ^{−H} \=N	54
10	Me CI	N [∕] N ^{−H}	14

Reaction conditions: see Section 4.

^a Yields determined by ¹H NMR spectroscopy.

Table 5					
N-Arylation	of amides	with	substituted	aryl halides	



Entry	Aryl halide	Amide	Yield ^a (%)
1	Me O	O NH ₂	73
2	Me O Br	NH ₂	31
3	Me O-CI	O NH ₂	10
4	MeO	O NH ₂	<1
5	Me O	O N-H	100
6	Me O Br	O N-H	<1

Reaction conditions: see Section 4.

^a Yields determined by ¹H NMR spectroscopy.

only possible coupling partner. Such a lower activity could be due to partial catalyst deactivation under the employed reaction conditions. In fact, it has been proved that the cross-coupling between aryl iodides and amides catalyzed by copper(I) complexes with chelating diamine ligands is suppressed by multiple coordination to the catalyst of amidate anions, which are formed under reaction conditions; formation of such a catalytically inactive complex can be avoided by working with excess ligand (>5 equiv with respect to copper), which promotes partial dissociation of the amidate anions thereby increasing the reaction rate.³⁸ Since we work with a preformed copper complex catalyst and therefore with a stoichiometric amount of ligand, it is plausible that such a deactivation mechanism may be operating in our case as well.

The last substrate class, which was investigated in the present study were phenols. The results are reported in Table 6. The reactivity of phenols with catalyst (2) appears to be comparable with that of azoles. As expected, the more sterically hindered 5-isopropyl-3-methylphenol was found to be slightly less reactive than the less sterically hindered p-cresol, giving somewhat lower yields with the more activated aryl halide partners.

Table 6

O-Arylation of phenols with substituted aryl halides

RХ +ОН	$\frac{[Cu] 3 \text{ mol}\%}{Cs_2CO_3, DMSO}$ T = 100 °C, 24h	R
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Reaction conditions: see Section 4.

^a Yields determined by ¹H NMR spectroscopy.

3. Conclusions

In conclusion we have developed a trinuclear copper(I) carbene complex that displays good catalytic efficiency in the Ullmann-type arylation reaction of azoles and phenols. The catalyst is capable of converting aryl iodides, bromides or even activated chlorides at a comparatively low reaction temperature (100 °C). Furthermore, different azoles such as pyrazole, imidazole or 1,2,4-triazole are converted with comparable efficiency. We are currently engaged in further extending the field of application of our catalyst, as well as in gaining insight into its mechanism of action, in order to find a rational explanation of its peculiar features, first of all the unexpected sensitivity to the nature of the aryl substituent.

4. Experimental section

4.1. General comments

All manipulations were carried out using standard Schlenk techniques under an atmosphere of dry argon or dinitrogen. The reagents were purchased by Aldrich or Merck as highpurity products and generally used as received. All solvents were dried by standard procedures and distilled under dinitrogen immediately prior to use. Complex $[CuBr(PPh_3)_3]^{39}$ was prepared according to literature procedures. NMR spectra were recorded on a Bruker Avance 300 MHz (300.1 MHz for ¹H and 75.5 MHz for ¹³C); chemical shifts (δ) are reported in units of parts per million relative to the residual solvent signals. IR spectra were run on a Bruker Tensor27; mass spectra were obtained with a Finningan LCQ, using the ESI-MS technique.

XPS spectra were recorded using a Perkin-Elmer PHI 5600 ci spectrometer with a standard Al Ka source (1486.6 eV) working at 350 W. The working pressure was less than 1×10^{-8} Pa. The spectrometer was calibrated by assuming the binding energy (BE) of the Au $4f_{7/2}$ line to lie at 84.0 eV with respect to the Fermi level. Extended spectra (survey) were collected in the range 0-1350 eV (187.85 eV pass energy, 0.4 eV step, 0.05 s step^{-1}). Detailed spectra were recorded for the following regions: C 1s, O 1s, F 1s, Cu 2p and Cu LMM (11.75 eV pass energy, 0.1 eV step, 0.1 s step⁻¹). The standard deviation in the BE values of the XPS line is 0.10 eV. To take into consideration charging problems the C 1s peak at 285.0 eV was considered and the peak's BE differences were evaluated. The sample for the XPS analysis was processed as a pellet by pressing the catalyst powder at ca. 7×10^6 Pa for 10 min; the pellet was then evacuated for 12 h at ca. 1×10^3 Pa before measurement.

4.2. Synthesis of hydrotris(3-methyl-imidazolium-1-yl)borate bis(tetrafluoroborate)

The salt was prepared following a literature procedure,²⁹ modified in the purification step. A suspension of trimethyloxonium tetrafluoroborate (9.60 mmol, 20% excess) in 30 ml of dry CH_2Cl_2 was added in small portions to a suspension of hydrotris(1-imidazolyl)borate (2.0 g, 7.93 mmol) in 20 ml of dry CH₂Cl₂. The resulting mixture was left under stirring overnight, then the solvent was decanted, giving a white slurry. The crude product was washed with dry EtOH (2×10 mL), dry diethyl ether (2×10 mL), and finally dried under vacuo. The residue was treated with boiling methanol and the mixture was filtered to remove KBF₄ salts; the solution was concentrated to small volume and treated with diethyl ether (20 mL), yielding the analytically pure tris(imidazolin)borate as a white precipitate, which was filtered and dried in vacuo. Anal. Calcd for C₁₂H₁₉B₃F₈N₆: C, 33.36; H, 4.43; N, 19.46. Found: C, 33.33; H, 4.40; N, 19.46. ¹H NMR (DMSO-*d*₆): δ 3.82 (s, 3H, CH₃), 7.51 (s, 1H, CH=CH), 7.73 (s, 1H, CH=CH), 8.81 (s, 1H, NCHN).

4.3. Synthesis of bis[hydrotris(3-methyl-imidazolin-2-ylidene-1-yl)borate]tricopper(I) tetrafluoroborate (2)

A solution of *n*-BuLi in hexane (2 mL, 3.2 mmol) was added with stirring to a suspension of hydrotris(3-methyl-imidazolium-1-yl)borate bis(tetrafluoroborate) (460 mg, 1.06 mmol) in 15 mL of dry diethyl ether at -78 °C. The suspension was stirred overnight and allowed to warm to room temperature to give a light yellow suspension, which was added in portions to a solution of [CuBr(PPh₃)₃] (1.48 g, 1.60 mmol) in dry THF (20 mL) at -78 °C. The mixture was allowed to warm to room temperature overnight to give a light blue/green suspension, which was filtered. The resulting solid was washed several times with dry THF (5×10 mL), dry diethyl ether $(5 \times 5 \text{ mL})$, and dried in vacuo, giving 483 mg of (2) as a white solid. ¹H NMR (DMSO-*d*₆): δ 3.38 (s, 3H, CH₃), 7.16 (s, 1H, CH=CH), 7.26 (s, 1H, CH=CH). ¹³C NMR (DMSO-*d*₆): δ 37.2 (CH₃), 121.0 and 126.1 (CH=CH), 176.7 (NCN). MS (ESI, (*m/z*, rel intensity)): 701.4 (100, M⁺). FTIR (KBr, cm^{-1}): 1642, 1442, 1197, 1058.

Although the NMR and ESI-MS data for various catalyst batches indicated a spectroscopically pure product, only occasionally contaminated with some residual triphenylphosphine, we were unable to obtain satisfactory elemental analysis for (2). Anal. Calcd C, 45.23; H, 5.06; N, 26.37. Found: C, 31.69; H, 3.37; N, 14.54. The observed values were found to fit roughly with a sample containing approximately 0.25 mol PPh₃, 0.5 mol LiBF₄, and 3 mol LiBr per mol of (2). Anal. Calcd for the mixture: C, 29.47; H, 3.10; N, 14.47.

4.4. General procedure for C–N and C–O coupling reaction

The required amount of complex (2) (1 mol %, 3 mol % [Cu] determined on the real amount of copper present in each sample), the aryl halide (1.0 mmol), the base (2.0 mmol), the nitrogen- or oxygen-containing substrate (1.5 mmol), and 3 mL of solvent were placed in a Schlenk tube, previously evacuated and filled with argon. The resulting mixture was heated under stirring to 100 °C for 24 h and subsequently cooled to room temperature, diluted with dichloromethane (10 mL), and filtered. The filtrate was washed with a 5% w/w aqueous KHCO₃ solution (2×10 mL) and water (2×10 mL), and finally dried over MgSO₄. The solvent was removed in vacuo to yield

the crude product, which was analyzed by NMR to determine the yield. The products were identified by comparison with characterization data found in literature.^{14b,d,17k}

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References and notes

- 1. *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed.; de Meijere, A., Diederich, F., Eds.; Wiley-VCH: Weinheim, 2004.
- (a) Beletskaya, I. P.; Cheprakov, A. V. Chem. Rev. 2000, 100, 3009; (b) Whitcombe, N. J.; Hii, K. K.; Gibson, S. E. Tetrahedron 2001, 57, 7449.
- (a) Miyaura, N.; Suzuki, A. Chem. Rev. 1995, 95, 2457; (b) Suzuki, A. J. Organomet. Chem. 1999, 576, 147.
- (a) Buchwald, S. L. Acc. Chem. Res. 1998, 31, 805; (b) Hartwig, J. F. Acc. Chem. Res. 1998, 31, 853; (c) Schlummer, B.; Scholz, U. Adv. Synth. Catal. 2004, 346, 1599 and reference cited therein.
- 5. Farina, V. Adv. Synth. Catal. 2004, 346, 1553.
- (a) Netherton, M. R.; Fu, G. C. Adv. Synth. Catal. 2004, 346, 1525; (b) Tamao, K. J. Organomet. Chem. 2002, 653, 23; (c) Desmaerts, C.; Schneider, R.; Fort, Y. J. Org. Chem. 2002, 67, 3029; (d) Lipshutz, B. H. Adv. Synth. Catal. 2001, 343, 313; (e) Wolfe, J. P.; Buchwald, S. L. J. Am. Chem. Soc. 1997, 119, 6054; (f) Grushin, V. V.; Alper, H. Chem. Rev. 1994, 94, 1047.
- (a) Beletskaya, I. P.; Cheprakov, A. V. Coord. Chem. Rev. 2004, 248, 2337; (b) Ley, S. V.; Thomas, A. W. Angew. Chem., Int. Ed. 2003, 42, 5400; (c) Kunz, K.; Scholz, H.; Ganzer, D. Synlett 2003, 2428; (d) Finet, J. P.; Fedorov, A. Y.; Combes, S.; Boyer, G. Curr. Org. Chem. 2002, 6, 597; (e) Hassan, J.; Sevignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. Chem. Rev. 2002, 102, 1359.
- 8. Ullmann, F. Chem. Ber. 1903, 36, 2389.
- (a) Goldberg, I. Ber. Dtsch. Chem. Ges. 1906, 39, 1691; (b) Goldberg, I. Ber. Dtsch. Chem. Ges. 1907, 40, 4541.
- 10. Lindley, J. Tetrahedron 1984, 40, 1433.
- (a) Chan, D. M. T.; Monaco, K. L.; Wang, R.-P.; Winters, M. P. *Tetrahedron Lett.* **1998**, *39*, 2933; (b) Evans, D. A.; Katz, J. L.; West, T. R. *Tetrahedron Lett.* **1998**, *39*, 2937; (c) Lam, P. Y. S.; Clark, C. G.; Saubern, S.; Adams, J.; Winters, M. P.; Chan, D. M. T.; Combs, A. *Tetrahedron Lett.* **1998**, *39*, 2941; (d) Cundy, D. J.; Forsyth, S. A. *Tetrahedron Lett.* **1998**, *39*, 7979.
- (a) Collman, J. P.; Zhong, M. Org. Lett. 2000, 2, 1233; (b) Collman, J. P.; Zhong, M.; Zeng, L.; Costanzo, S. J. Org. Chem. 2001, 66, 1528; (c) Collman, J. P.; Zhong, M.; Zeng, L.; Costanzo, S. J. Org. Chem. 2001, 66, 7892; (d) Antilla, J. C.; Buchwald, S. L. Org. Lett. 2001, 3, 2077; (e) Lam, P. Y. S.; Vincent, G.; Clark, C. G.; Deudon, S.; Jadhav, P. K. Tetrahedron Lett. 2001, 42, 3415; (f) Lam, P. Y. S.; Vincent, G.; Bonne, D.; Clark, C. G. Tetrahedron Lett. 2003, 44, 4927; (g) Biffis, A.; Filippi, F.; Palma, G.; Lora, S.; Maccà, C.; Corain, B. J. Mol. Catal. A: Chem. 2003, 203, 213; (h) Chiang, G. C. H.; Olsson, T. Org. Lett. 2004, 6, 3079; (i) Moessner, C.; Bolm, C. Org. Lett. 2005, 7, 2667; (j) Strouse, J. J.; Jeselnik, M.; Tapaha, F.; Jonsson, C. B.; Parker, W. B.; Arterburn, J. B. Tetrahedron Lett. 2005, 46, 5699.
- (a) Lan, J.-B.; Chen, L.; Yu, X.-Q.; You, J.-S.; Xie, R.-G. *Chem. Commun.* **2004**, 188; (b) Lan, J.-B.; Zhang, G.-L.; Yu, X.-Q.; You, J.-S.; Chen, L.;
 Yan, M.; Xie, R.-G. *Synlett* **2004**, 1095.
- (a) Marcoux, J.-F.; Doye, S.; Buchwald, S. L. J. Am. Chem. Soc. 1997, 119, 10539; (b) Klapars, A.; Huang, X.; Buchwald, S. L. J. Am. Chem.

Soc. 2002, 124, 7421; (c) Antilla, J. C.; Klapars, A.; Buchwald, S. L.
J. Am. Chem. Soc. 2002, 124, 11684; (d) Antilla, J. C.; Baskin, J. M.;
Barder, T. E.; Buchwald, S. L. J. Org. Chem. 2004, 69, 5578; (e) Shafir,
A.; Buchwald, S. L. J. Am. Chem. Soc. 2006, 128, 8742; (f) Shafir, A.;
Lichtor, P. A.; Buchwald, S. L. J. Am. Chem. Soc. 2007, 129, 3490.

- (a) Ma, D.; Zhang, Y.; Yao, J.; Wu, S.; Tao, F. J. Am. Chem. Soc. 1998, 120, 12459; (b) Zhang, H.; Cai, Q.; Ma, D. J. Org. Chem. 2005, 70, 5164 and references cited therein; (c) Cai, Q.; Zou, B.; Ma, D. Angew. Chem., Int. Ed. 2006, 45, 1276.
- (a) Cristau, H.-J.; Cellier, P. P.; Spindler, J.-F.; Taillefer, M. *Chem.—Eur. J.* **2004**, *10*, 5607 and references cited therein; (b) Cristau, H.-J.; Cellier, P. P.; Spindler, J.-F.; Taillefer, M. *Eur. J. Org. Chem.* **2004**, 695; (c) Ouali, A.; Spindler, J.-F.; Cristau, H.-J.; Taillefer, M. *Adv. Synth. Catal.* **2006**, *348*, 499.
- 17. Selected recent examples: (a) Haider, J.; Kunz, K.; Scholz, U. Adv. Synth. Catal. 2004, 346, 717; (b) Xu, L.; Zhu, D.; Wu, F.; Wang, R.; Wan, B. Tetrahedron 2005, 61, 6553; (c) Kuil, M.; Bekedam, K.; Visser, G. M.; van den Hoogenband, A.; Terpstra, J. W.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; van Strijdonck, G. P. F. Tetrahedron Lett. 2005, 46, 2405; (d) Wang, Z.; Bao, W.; Jiang, Y. Chem. Commun. 2005, 2849; (e) Manbeck, G. F.; Lipman, A. J.; Stockland, R. A., Jr.; Freidl, A. L.; Hasler, A. F.; Stone, J. J.; Guzei, I. A. J. Org. Chem. 2005, 70, 244; (f) Liu, L.; Frohn, M.; Xi, N.; Dominguez, C.; Hungate, R.; Reider, P. J. J. Org. Chem. 2005, 70, 10135; (g) Guo, X.; Rao, H. H.; Fu, H.; Jiang, Y. Y.; Zhao, Y. F. Adv. Synth. Catal. 2006, 348, 2197; (h) de Lange, B.; Lambers-Verstappen, M. H.; Schmieder-van de Vondervoort, L.; Sereinig, N.; De Rijk, R.; De Vries, A. H. M.; De Vries, J. G. Synlett 2006, 3105; (i) Jiang, D.; Fu, H.; Jiang, Y.; Zhao, Y. J. Org. Chem. 2007, 72, 672; (j) Zhu, L.; Cheng, L.; Zhang, Y.; Xie, R.; You, J. J. Org. Chem. 2007, 72, 2737; (k) Lv, X.; Bao, W. J. Org. Chem. 2007, 72, 3863.
- 18. Son, S. U.; Park, I. K.; Park, J.; Hyeon, T. Chem. Commun. 2004, 778.
- (a) Choudary, B. C.; Sridhar, C.; Kantam, M. L.; Venkanna, G. T.; Sreedhar, B. *J. Am. Chem. Soc.* **2005**, *127*, 9948; (b) Kantam, M. L.; Yadav, J.; Laha, S.; Sreedhar, B.; Jhab, S. *Adv. Synth. Catal.* **2007**, *349*, 1938.
- Lohmann, S.; Andrews, S. P.; Burke, B. J.; Smith, M. D.; Attfield, J. P.; Tanaka, H.; Kaneko, K.; Ley, S. V. Synlett 2005, 1291.
- (a) Tubaro, C.; Biffis, A.; Basato, M.; Benetollo, F.; Cavell, K. J.; Ooi, L. L. *Organometallics* 2005, 24, 4153; (b) Tubaro, C.; Biffis, A.; Gonzato, C.; Zecca, M.; Basato, M. J. Mol. Catal. A: Chem. 2006, 248, 93; (c) Biffis, A.; Tubaro, C.; Buscemi, G.; Basato, M. Adv. Synth. Catal. 2008, 350, 189.
- (a) N-Heterocyclic Carbenes in Transition Metal Catalysis; Glorius, F., Ed.; Topics in Organometallic Chemistry; Springer: Heidelberg, 2007; Vol. 21; (b) N-Heterocyclic Carbenes in Synthesis; Nolan, S. P., Ed.; Wiley-VCH: Weinheim, 2006; (c) Herrmann, W. A. Angew. Chem., Int. Ed. 2002, 41, 1290; (d) Herrmann, W. A.; Weskamp, T.; Böhm, V. P. W. Adv. Organomet. Chem. 2001, 48, 1; (e) Jafarpour, L.; Nolan, S. P. Adv. Organomet. Chem. 2001, 46, 181; (f) Bourissou, D.; Guerret, O.; Gabbaï, F. P.; Bertrand, G. Chem. Rev. 2000, 100, 39.
- 23. Fürstner, A. Angew. Chem., Int. Ed. 2000, 39, 3012.
- (a) Herrmann, W. A.; Öfele, K.; v. Preysing, D.; Schneider, S. J. Organomet. Chem. 2003, 687, 229; (b) Yang, C.; Lee, H. M.; Nolan, S. P. Org. Lett. 2001, 3, 1511; (c) Stauffer, S. R.; Lee, S.; Stambuli, J. P.; Hauck, S. I.; Hartwig, J. F. Org. Lett. 2000, 2, 1423.
- Markó, I. E.; Stérin, S.; Buisine, O.; Mignani, G.; Branlard, P.; Tinant, B.; Declercq, J.-P. Science 2002, 298, 204.
- (a) Jackstell, R.; Harkal, S.; Jiao, H. J.; Spannenberg, A.; Borgmann, C.; Rottger, D.; Nierlich, F.; Elliot, M.; Niven, S.; Cavell, K. J.; Navarro, O.; Viciu, M. S.; Nolan, S. P.; Beller, M. *Chem.—Eur. J.* **2004**, *10*, 3891; (b) Jackstell, R.; Andreu, M. G.; Frisch, A.; Selvakumar, K.; Zapf, A.; Klein, H.; Spannenberg, A.; Rottger, D.; Briel, O.; Karch, R.; Beller, M. *Angew. Chem., Int. Ed.* **2002**, *41*, 986.
- Jensen, D. R.; Schultz, M. J.; Mueller, J. A.; Sigman, M. S. Angew. Chem., Int. Ed. 2003, 42, 3810.
- (a) Mata, J. A.; Poyatos, M.; Peris, E. Coord. Chem. Rev. 2007, 251, 841;
 (b) Peris, E.; Crabtree, R. H. Coord. Chem. Rev. 2004, 248, 2239.
- (a) Fränkel, R.; Kernbach, U.; Bakola-Christianopoulou, M.; Plaia, U.; Suter, M.; Ponikwar, W.; Nöth, H.; Moinet, C.; Fehlhammer, W. P. J. Organomet. Chem. 2001, 617–618, 530; (b) Kernbach, U.; Ramm, M.; Luger, P.; Fehlhammer, W. P. Angew. Chem., Int. Ed. 1996, 35,

310; (c) Fränkel, R.; Birg, C.; Kernbach, U.; Habereder, T.; Nöth, H.; Fehlhammer, W. P. Angew. Chem., Int. Ed. 2001, 40, 1907.

- (a) Hu, X.; Castro-Rodriguez, I.; Meyer, K. Organometallics 2003, 22, 3016; (b) Hu, X.; Tang, Y.; Gantzel, P.; Meyer, K. Organometallics 2003, 22, 612; (c) Hu, X.; Castro-Rodriguez, I.; Olsen, K.; Meyer, K. Organometallics 2004, 23, 755; (d) Hu, X.; Castro-Rodriguez, I.; Meyer, K. Chem. Commun. 2004, 2164; (e) Hu, X.; Castro-Rodriguez, I.; Meyer, K. J. Am. Chem. Soc. 2003, 125, 12237; (f) Hu, X.; Castro-Rodriguez, I.; Meyer, K. J. Am. Chem. Soc. 2004, 126, 16322; (h) Mas-Marza, E.; Peris, E.; Castro-Rodriguez, I.; Meyer, K. J. Organometallics 2005, 24, 3158; (i) Hu, X.; Meyer, K. J. Organomet. Chem. 2005, 690, 5474.
- (a) Forshaw, A. P.; Bontchev, R. P.; Smith, J. M. Inorg. Chem. 2007, 46, 3792; (b) Cowley, R. E.; Bontchev, R. P.; Duesler, E. N.; Smith, J. M. Inorg. Chem. 2006, 45, 9771; (c) Nieto, I.; Cervantes-Lee, F.; Smith, J. M. Chem. Commun. 2005, 3811.
- 32. (a) Dias, H. V. R.; Jin, W. Tetrahedron Lett. 1994, 35, 1365; Nakai, H.; Tang, Y.; Gantzel, P.; Meyer, K. Chem. Commun. 2003, 24.

- There are several examples of this kind of clusters: (a) Churchill, M. R.; Bezman, S. A.; Osborn, J. A.; Wormald, J. *Inorg. Chem.* **1972**, *11*, 1818; (b) Wehman, E.; van Koten, G.; Jastrzebski, J. T. B. H.; Rotteveel, M. A.; Stam, C. H. *Organometallics* **1988**, *7*, 1477.
- 34. Fränkel, R. Ph.D. Thesis, Technische Universität, München, 2001.
- (a) Panzner, G.; Egert, B.; Schmidt, H. P. *Surf. Sci.* 1985, *151*, 400; (b) NIST X-ray Photoelectron Spectroscopy Database, NIST Standard Reference Database 20, Version 3.4 (Web Version).
- Lam, M. H. W.; Tang, Y.-Y.; Fung, K.-M.; You, X.-Z.; Wong, W.-T. Chem. Commun. 1997, 957.
- (a) Arentsen, K.; Caddick, S.; Cloke, F. G. N. *Tetrahedron* 2005, *61*, 9710;
 (b) Parisel, S. L.; Adrio, L. A.; Pereira, A. A.; Perez, M. M.; Vila, J. M.; Hii, K. K. *Tetrahedron* 2005, *61*, 9822.
- (a) Strieter, E. R.; Blackmond, D. G.; Buchwald, S. L. J. Am. Chem. Soc.
 2005, 127, 4120; (b) Zhang, S.-L.; Liu, L.; Fu, Y.; Guo, Q.-X. Organometallics 2007, 26, 4546.
- Gujadhur, R.; Venkantaraman, D.; Kintigh, J. T. Tetrahedron Lett. 2001, 42, 4791.