Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron
Tetrahedron 64 (2008) 2471–2479
www.elsevier.com/locate/tet

Bis(μ-iodo)bis((−)-sparteine)dicopper(I): versatile catalyst for direct N-arylation of diverse nitrogen heterocycles with haloarenes

H. Maheswaran [a,*], G. Gopi Krishna [a], K. Leon Prasanth [a], V. Srinivas [a], G. Krishna Chaitanya [b], K. Bhanuprakash [b]

[a] *Homogeneous Catalysis Wing, IPC Division, Indian Institute of Chemical Technology, Hyderabad 500 007, India*
[b] *Quantum Chemistry Wing, IPC Division, Indian Institute of Chemical Technology, Hyderabad 500 007, India*

Received 28 August 2007; received in revised form 26 November 2007; accepted 20 December 2007
Available online 24 December 2007

Abstract

The easy-to-prepare dimeric bis(μ-iodo)bis((−)-sparteine)dicopper(I) complex is shown to be a versatile catalyst for N-arylation of number of NH−heterocycles with structurally divergent aryl halides including activated aryl chloride substrates under mild conditions. The DFT studies not only provide structural insights into square-pyramidal Cu(III) intermediate complexes derived from (−)-sparteine, but also highlight the important role of sterically demanding (−)-sparteine ligand framework in promoting activation of aryl−chlorine bonds for N-arylation of imidazoles.

1. Introduction

N-Arylheterocycles are prevalent motifs in numerous natural products and in biologically active pharmaceuticals.[1] The most promising method for their synthesis is copper(I) catalyzed Ullmann-type coupling in the presence of basic nitrogen ligands.[2] Since the initial report by Buchwald,[3] substantial progress has been made on the direct copper(I) catalyzed C−N coupling reactions,[2b,c,4,5] for the synthesis of *N*-arylheterocycles. The key to the success in this area is the in situ utilization of special nitrogen ligand additives along with copper(I) precursor salts as catalysts. Frequently used ligand additives include 1,2-diamines,[4a−d] 1,10-phenanthroline/PPh_3,[6] 4,7-dichloro-1,10-phenanthroline,[7] Schiff-bases,[8] amino acids,[9] DMEDA,[10] 8-hydroxyquinoline,[11] aminoarenethiol,[12] oximephosphineoxides,[13] pipecolinic acid,[14] and pyrrolidinylmethylimidazole.[15] Very recently, Buchwald has disclosed 4,7-dimethoxy-1,10-phenanthroline as the most efficient nitrogen ligand for Cu-catalyzed N-arylation of imidazole and benzimidazole with aryl and heteroaryl iodides/bromides in combination with PEG and Cs_2CO_3, which exhibits high functional group tolerance.[4f,g] However, only a few ligand systems reported to date tolerate reactions with sterically hindered substrate combinations. More importantly, most of the studies reported employ either iodo- or bromoarenes as substrates. The coupling of NH−heterocycles with cheaper and less reactive aryl chloride substrates still remains a challenging problem. In addition, some of the very efficient nitrogen ligands are rather expensive, and may require multi-step protocols for their synthesis.[16] Therefore, it is very important to develop both cost-effective and efficient ligand/catalyst systems that facilitate direct C−N cross-coupling reactions. Herein, we report our studies using catalytic amounts of copper(I) salts with readily available quinolizidine alkaloid (−)-sparteine as nitrogen ligand.

We also conceived evaluating (−)-sparteine as nitrogen ligand for several other reasons. An important reason is that the tertiary nitrogen atoms of fused ring systems of (−)-sparteine are poor sigma-donors in general, and are sterically hindered. Our group has shown lately that chelation of (−)-sparteine to copper results in precise counteranion-dependent stereochemical outcomes, and that contributes to significant

* Corresponding author. Tel.: +91 40 27193510; fax: +91 40 27160921.
E-mail address: maheswaran_dr@yahoo.com (H. Maheswaran).

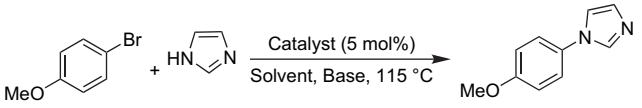
0040-4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.12.050

differences in their reactivities and selectivities in asymmetric C–C bond forming reactions.[17] It has also been demonstrated that ligands having poor sigma-donor characteristics result in larger thermodynamic stabilization of catalytically active lower valent Cu(I) species.[18] Thus, it was envisioned that the use of (−)-sparteine as ligand may result in good catalytic activities for copper catalyzed C–N coupling reactions, in particular, with difficult substrates such as chloroarenes. Another reason is that, unlike many nitrogen ligands used for cross-coupling reactions, information concerning both the aggregation states and coordination geometries as well as X-ray crystal structures of Cu(I)/(−)-sparteine complexes is well-understood.[19,20] For example, the direct reaction between CuX salts and (−)-sparteine in equimolar amounts yields a stable and discrete dimeric [Cu_2X_2((−)-spa)$_2$] complexes with a Cu_2X_2 core.[20] In contrast, with excess of copper(I) salts, i.e., an initial CuX/(−)-sparteine ratio of 2:1, results in the formation of discrete [Cu_4X_4(spa)$_2$] complexes, with a laddered Cu_4X_4 core.[20] Thus, this valuable information may enable direct utilization of stable preformed Cu(I)–(−)-sparteine complexes with a well-defined structure as catalysts for the cross-coupling reactions without resorting to in situ conditions.[21]

2. Results and discussion

First, 4-bromoanisole and imidazole were chosen as model substrates for catalyst screening studies, and these substrates were subjected to various reaction conditions with (−)-sparteine as the ligand under in situ conditions. As seen in Table 1, different copper(I) salts such as CuI, CuCl, and Cu_2O promote coupling reactions for model substrates, with K_2CO_3 as base in DMSO at 115 °C (entries 1–3). The results show that the choice of copper precursor has a profound effect on the reaction as both CuCl and Cu_2O afforded only moderate yields for coupled product *N*-4-methoxyphenylimidazole (65 and 56%, respectively). However, with CuI, this product was obtained in excellent yield (92%). Among the various bases screened, both K_2CO_3 and Cs_2CO_3 gave comparable yields (92 and 89%), while K_3PO_4 gave poor yields (65%) (entries 1, 7, and 8) of *N*-4-methoxyphenylimidazole. Similarly, the choice of solvent also plays an important role; for example, reactions in DMSO gave superior yields (92%) for the coupled product in comparison to those of DMF, NMP, and xylene (entries 1, 4, 5, and 6). As discussed earlier, the preformed bis(μ-iodo)bis((−)-sparteine)dicopper(I) complex containing a Cu_2X_2 core was synthesized and characterized by using a modified literature procedure[20] (also see Supplementary data). This preformed complex was directly used as catalyst (5 mol % relative to the substrate) for the reaction between standard substrates, which provides yields as high as 85% in 12 h for desired coupled product (entry 9). This reaction is highly reproducible and gave excellent yields that are comparable to those obtained under in situ conditions with equimolar amounts of Cu(I) and (−)-sparteine (entry 1).

Table 1
Screening of reaction parameters for copper(I) catalyzed N-arylation of NH–heterocycles with (−)-sparteine[a]



Entry	Catalyst	Solvent	Base	Time/h	Yield[b]/%
1	CuI	DMSO	K_2CO_3	12	92
2	CuCl	DMSO	K_2CO_3	12	65
3	Cu_2O	DMSO	K_2CO_3	12	56
4	CuI	DMF	K_2CO_3	12	73
5	CuI	NMP	K_2CO_3	12	68
6	CuI	Xylene	K_2CO_3	12	37
7	CuI	DMSO	Cs_2CO_3	12	89
8	CuI	DMSO	K_3PO_4	12	65
9[c]	Cu_2I_2(spa)$_2$	DMSO	K_2CO_3	12	85

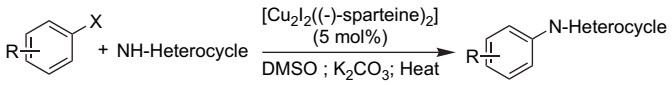
[a] Reactions (entries 1–8) were performed under in situ conditions on a 1.0 mmol scale with CuX (0.1 mmol, 10 mol %), bromoanisole (1.0 mmol), (−)-sparteine (0.1 mmol, 10 mol %), imidazole (1.2 mmol), K_2CO_3 (2 mmol), and 5 mL of DMSO at 115 °C.
[b] Values are isolated yields after chromatographic purification.
[c] Reaction (entry 9) was performed with 5 mol % of preformed bis-(μ-iodo)bis((−)-sparteine)dicopper(I) catalyst by employing similar reaction conditions.

Optimized reaction conditions were further extended to the reactions of diverse aryl halide substrates with nitrogen heterocycles, using 5 mol % of preformed CuI/(−)-sparteine catalyst, and the results are listed in Table 2. As can be seen, this protocol is rather general, as it is applicable for the reactions of a variety of electron-rich and electron-deficient aryl bromides as well as aryl iodides with NH–heterocycles such as imidazole, benzimidazole, and pyrazole. The reaction of aryl iodides was rather fast, and their coupling reactions with imidazole, benzimidazole, and pyrazole substrates gave almost quantitative yields within 5–7 h (entries 1–4). Understandably, aryl bromide substrates require slightly longer reaction times as reactions of bromoanisole with imidazole and pyrazole take up to 8 h to afford the coupling products in 89 and 82% yields, respectively (entries 6 and 7).

As illustrated in Table 2, electron-rich bromoarenes like *p*-bromoanisole, *p*-bromotoluene, and *m*-bromoanisole take even longer reaction times (up to 13 h) to afford coupling products in >80% yields (entries 8–12). In contrast, reactions of those aryl bromides involving electron-deficient bromoarene substrates (containing electron-withdrawing groups such as *p*-COMe, *p*-CHO, *p*-NO_2, and *p*-CN groups) proceeded much faster (6–8 h) to provide good to excellent yields for corresponding adducts (entries 14–21). No side products including hydrolyzed products were obtained under reaction conditions. In the hope of broadening the scope of N-arylation protocol, we decided to check the efficiency of our catalyst system with less reactive aryl chloride substrates. As seen in Table 2, the reactions of nitrogen heterocycles with various aryl chloride substrates having electron-withdrawing groups proceed smoothly, albeit at slightly higher reaction temperature (125 °C).

Substrates containing *p*-NO_2, *p*-CN, and *p*-CF_3 groups gave excellent yields (83–92%) for the corresponding *N*-arylated adducts, and the reaction times range from 12 to 19 h (entries 22–29). Unlike aryl bromides, the aryl chloride substrates containing the *p*-COMe and *p*-CHO substituents gave slightly

Table 2
N-Arylation of NH–heterocycles with various haloarenes catalyzed by preformed bis(μ-iodo)bis((−)-sparteine)dicopper(I)[a]



Entry	R	X	HN–Het	*T*/°C	Time/h	Yield[b]/%
1	H	I	Im	115	5	95
2	*p*-OMe	I	Im	115	7	95
3	*p*-OMe	I	BzIm	115	7	95
4	*p*-OMe	I	Py	115	7	91
5	*o*-OMe	I	Im	115	12	92
6	H	Br	Im	115	8	89
7	H	Br	Py	115	8	82
8	*p*-OMe	Br	Im	115	12	85
9	*p*-OMe	Br	BzIm	115	13	88
10	*p*-OMe	Br	Py	115	12	82
11	*m*-OMe	Br	Im	115	12	86
12	*p*-Me	Br	Im	115	12	88
13	*o*-OMe	Br	Im	115	24	70
14	*p*-COMe	Br	Im	115	7	97
15	*p*-COMe	Br	BzIm	115	8	92
16	*p*-CHO	Br	Im	115	8	91
17	*p*-CHO	Br	Py	115	8	77
18	*p*-CHO	Br	BzIm	115	8	90
19	*p*-NO_2	Br	Im	115	6	96
20	*p*-NO_2	Br	BzIm	115	6	95
21	*p*-CN	Br	Im	115	7	92
22	*p*-NO_2	Cl	BzIm	110	12	83
23	*p*-NO_2	Cl	Im	125	12	91
24	*o*-NO_2	Cl	Im	125	12	92
25	*p*-CN	Cl	Im	125	14	89
26	*p*-CN	Cl	BzIm	125	14	86
27	*o*-CN	Cl	Im	125	14	87
28	*o*-CN	Cl	BzIm	125	16	82
29	*p*-CF_3	Cl	Im	125	15	91
30	*p*-COMe	Cl	Im	125	17	79
31	*p*-COMe	Cl	BzIm	125	19	75
32	*p*-CHO	Cl	Im	125	18	75
33	*p*-CHO	Cl	Py	125	18	65
34	*p*-CHO	Cl	BzIm	125	19	77
35	H	Cl	Im	125	24	<10[c]

[a] All reactions were performed on a 1.0 mmol scale with 5 mol % of preformed bis(μ-iodo)bis((−)-sparteine)dicopper(I) complex, K_2CO_3 (2 mmol), aryl halide (1.0 mmol), corresponding HN–Het (1.2 mmol), and 5 mL of DMSO at the specified temperature. Abbreviations: Im=imidazole, BzIm=benzimidazole, and Py=pyrazole.

[b] Values are isolated yields after chromatographic purification.

[c] Value corresponds to the ^{1}H NMR yield obtained from the crude reaction mixture.

lower yields (65–79%) for the coupling products (entries 30–34). Notably, unactivated chlorobenzene substrate reacts very slowly with imidazole, and even after 24 h of reaction, gave very poor yield for the coupled product (entry 35). The present catalyst system also works efficiently for sterically hindered aryl halide substrates. For example, the reaction of *o*-substituted aryl iodides, aryl bromides, and activated aryl chloride substrates reacts smoothly with imidazole and afford excellent yields (entries 5, 13, 24, 27, and 28), although these reactions require longer reaction times (12–24 h) in comparison to their unhindered counterparts. However, as anticipated, electron-rich aryl chloride substrates (those containing electron-donating groups) did not react at all under our reaction conditions.

From the discussions above, the following generalizations can be easily made. First, electron-withdrawing groups enable cross-coupling reactions with NH–heterocycles to proceed faster than those of one containing electron-donating groups. Second, our protocol tolerates steric factors (*ortho*-substitution) in the aryl halide substrates. Unlike Pd(0) mediated protocols,[22] such tolerance to steric factors by copper is well known in C–N cross-coupling chemistry. This distinct feature could be related to mechanistic divergence in their chemistry as well as due to different nature of intermediates that are formed in the catalytic cycle.[23] Finally, more difficult aryl chloride substrates (activated) undergo cross-coupling with diverse NH–heterocycles such as pyrazole, imidazole, and benzimidazole in excellent yields.

To the best of our knowledge, this is the first N-arylation report with activated chloroarene substrates (Table 2; 13 substrate combinations in total) for use in direct cross-coupling methodology with NH–heterocycles under semi-homogeneous conditions. At present, only a few examples involving aryl chlorides' activation for copper catalyzed C–N bond formation with NH–heterocycles have been reported, which require either heterogeneous catalysts or nanoparticles based catalysts.[24] Therefore, bis(μ-iodo)bis((−)-sparteine)dicopper(I) represents a versatile catalyst system for direct N-arylation of NH–heterocycles with diverse aryl halide substrates under mild conditions. We attribute this enhanced efficiency to the unique ability of (−)-sparteine ligand; the rationale for its efficacy could be ascertained by gaining mechanistic insights into the reaction.

However, despite the wide spread use of copper catalyzed C–N coupling protocols, the reaction mechanism is not clearly understood to date. Indeed, pioneering contributions by Weingarten, Cohen, and Paine have demonstrated, using different experimental techniques, that the active catalytic species in the Ullmann-type coupling is indeed copper(I).[25] Among the classes of different mechanisms that have been proposed in the literature, a generally accepted mechanism is the one originally proposed by Cohen or its modified versions.[25d,26,4g,8] This mechanism involves a catalytic cycle in which the oxidative addition of copper(I) into the aryl–halogen bond results in the formation of 'four-coordinate Cu(III) intermediate', which then undergoes an exchange of the halide with the nucleophile (Nu), and subsequent reductive elimination to form the coupled product, and regenerate the active copper(I) species. Indeed, such a mechanism is very reasonable one because the chemistry of Cu(III) does not appear to be elusive any longer as plethora of publications with direct evidence for Cu(III) species are forthcoming in the literature.[27] Very recently, the intermediacy of Cu(III) complexes (with copper–carbon bonds) in copper catalyzed reactions has been elegantly demonstrated using solution-state NMR techniques.[28] Moreover, a number of stable copper(III) compounds containing copper–carbon bonds are known, which is evident from the pioneering contributions of Stack and co-workers, who have reported their formation by the activation of aryl C–H bonds by copper(II).[29]

There are still, however, some experimental details that do not appear to agree with Cu(III) intermediates in modified Ullmann reactions. First, most of the reported C–N coupling reactions involve the coupling of aryl iodides using either copper(I) or halo complexes of copper(I). Thus, the formation of Cu(III) intermediate in the presence of I^- has been suggested to be less likely or even *unprecedented*.[25g] This suggestion makes good sense because a relatively small Cu cation with a large positive charge (hard ion) is less likely to have strong interaction with relatively soft-iodide ions. However, it has been elegantly shown that auxiliary ligands play a much more important role for the stabilization of high valent oxidation states in their metal complexes.[30] This is clearly seen from the ability of corroles to stabilize the unusually high oxidation states of manganese like +5, and even +6. In fact, the stabilizing effect of the corrole macrocycle has been demonstrated to prepare 'even the iodo derivative of a Mn(IV) corrole'.[31] In this complex, iodide occupies apical position of slightly distorted square-pyramidal geometry.

Similarly, stable Cu(III) complexes of general formula, $[Cu^{III}(L)Cl]^+[ClO_4]^-$ with L being a monoanionic triazamacrocycle ligand, have been synthesized by Xifra and co-workers, by the activation of aryl C–H bonds present in the macrocycle by copper(II) complexes, followed by reaction with chloride anions. An X-ray crystal structure of this complex shows square-pyramidal geometry around copper with an axially coordinating Cl atom, with $[ClO_4]^-$ counter anions very weakly associated with metal center at a distance of 6–7 Å.[32] Therefore, formation of pentacoordinate catalytic Cu(III) intermediates with iodide ions or other halide ions is feasible under C–N cross-coupling conditions, particularly, when proper choice of nitrogen ligand additives is made.

Indeed, nitrogen ligands play a crucial role in promoting copper(I) catalyzed C–N cross-coupling reactions; a large number of efficient nitrogen ligand systems are known for this reaction. It is very likely that this reaction proceeds via the intermediacy of similar five-coordinate Cu(III) complexes containing at least one halide ion. Electrochemical measurements with square-pyramidal $[Cu^{III}(L)Cl]^+[ClO_4]^-$ complexes[32a] show that substitution of electron-withdrawing groups (NO_2) into the phenyl ring of the macrocycle results in a large peak splitting with significant anodic shifts in their $E_{1/2}$ values (−0.271 V), thus effecting greater stabilization of Cu(III) in the square-pyramidal geometry. This phenomenon could account for the higher reactivity of the electron-withdrawing aryl chlorides in the present study, provided that the intermediacy of similar five-coordinate Cu(III) species in the catalytic cycle is invoked.[33]

Furthermore, Cohen's proposition of 'four-coordinate Cu(III) intermediates' in the mechanistic cycle is very similar to those of Pd(0) catalyzed reactions, and is quite attractive based upon this similarity. However, present mechanistic understanding of Pd mediated cross-coupling chemistry has undergone revision from a text book mechanism involving four-coordinate Pd-oxidative addition intermediates to the viability of five-coordinate intermediates. For Heck reactions, the five-coordinate intermediates have been proposed via an Amatore–Jutand pathway by pre-coordination of an anion (Cl, OAc) to the palladium catalyst, PdL_2, followed by oxidative addition of aryl halides.[34] Similarly, recent studies with X-ray crystal structure studies of biarylmonophosphine derived Pd-oxidative-addition complexes have demonstrated existence of stable pentacoordinate palladium(II) complexes, which is very relevant to C–N coupling reactions.[35,36]

Herein, we wish to propose a plausible mechanism for N-arylation to account for our experimental observation that aryl chlorides form excellent substrates for cross-coupling with imidazole with Cu/(−)-sparteine catalyst system. As seen in Figure 1, we first propose that oxidative addition of

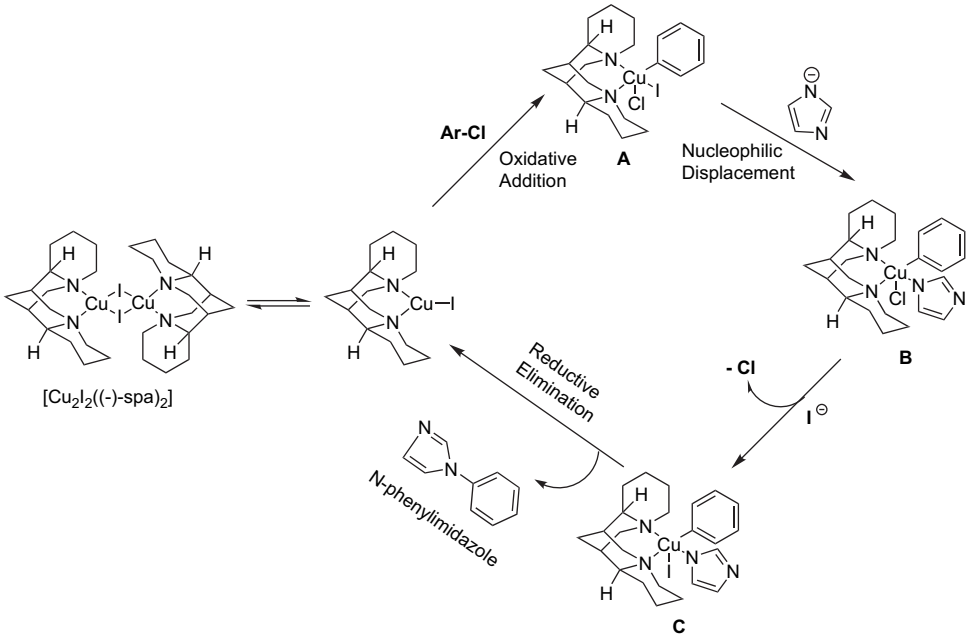


Figure 1. Proposed pentacoordinate Cu(III) intermediates in the mechanistic scheme for bis(μ-iodo)bis((−)-sparteine)dicopper(I) catalyzed N-arylation of imidazole using aryl chlorides.

aryl chlorides to Cu(I)/(−)-sparteine complex occurs, and that results in square-pyramidal Cu(III) intermediate **A**. We also propose that this intermediate, upon nucleophilic displacement reaction of iodide ion by imidazole anion, could result in intermediate **B**. It is to be noted that the structural features of Xifra's pentacoordinate $[Cu^{III}(L)Cl]^{+}[ClO_4]^{-}$ complexes are very similar to the proposed Cu(III) intermediate, **B** in particular, without counter anions (also see Supplementary data; page no. 19).

Despite numerous attempts employing various conditions, we have not been able to obtain X-ray quality single crystals on proposed Cu(III) complexes (**A** and **B**) for analysis by X-ray methods. Thus, we turned to computational approach involving DFT calculations using Amsterdam Density Functional Package (2006.01b)[37] to gather insights into the molecular structures of these complexes. Chlorobenzene was chosen for these computational studies. Several questions are prudent with respect to our findings: what are the stereochemical restrictions imposed by some important nitrogen ligands including (−)-sparteine in the coordination sphere of five-coordinate Cu(III) intermediates? What are their geometric parameters and binding energies? It is to be noted that five-coordinate species are remarkable in structural and computational chemistry, as they have no low energy geometry with stereochemically equivalent sites.[38]

With these objectives in mind, geometry optimizations were carried out for intermediate complexes **A** and **B** with TZ2P basis sets for neutral closed-shell singlet ground-state geometries without symmetry constraints to obtain various parameters using both BLYP and PW91 functionals. The results from these studies were then compared with those of similar intermediates derived from other nitrogen ligands such as 4,7-dihydroxy-1,10-phenanthroline[39] and *trans*-1,2-cyclohexyldiamine (with both *chair* and *boat* conformation in the cyclohexyl rings). These nitrogen ligands have been shown to be very effective for N-arylation of imidazole and pyrazole with bromo- and iodoarenes; hence, they were chosen for comparative computational studies.[40] Each additional nitrogen ligand chosen here for the comparative studies is excellent and very efficient indeed for N-arylation reaction in their own respects.

Figure 2 shows 3D representation of optimized molecular geometries for Cu(III) intermediates (**A** and **B**) derived from various nitrogen ligands. In line with Xifra's Cu(III) complexes, all the optimized structures display square-pyramidal geometry with a Cl atom occupying the axial position. Since this feature is seen in all the complexes, it is very likely that the chelating nitrogen ligand in the equatorial plane controls the position of Cl atom in their molecular structures. A particularly noteworthy aspect of these Cu(III) intermediates is present in their binding energies. As can be clearly seen, the difference in binding energies between intermediates **A** and **B**, $\Delta[(\Delta E)_B-(\Delta E)_A]$, as a measure of overall gain in energy, is very large when the nitrogen ligand is (−)-sparteine, which is −14.6 kcal/mol. The corresponding binding energy for 4,7-dihydroxy-1,10-phenanthroline Cu(III) intermediate is only −7.5 kcal/mol. Similar values of −8.4 and −8.6 kcal/mol were obtained for intermediates derived from *trans*-1,2-cyclohexyldiamine ligands having both *chair* and *boat* conformation in the cyclohexyl rings, respectively.

Another striking feature associated with the molecular structures of Cu(III) intermediates (**A** and **B**) is the inter atomic distances between the *ipso*-C atom (of Ph group) and I or N3 atom (of imidazole). Noticeably, (−)-sparteine containing intermediates (**A** and **B**) have much shorter inter atomic distances, 2.64 and 2.41 Å, respectively, which is very essential for coupled product formation via reductive elimination step. These important differences both in the geometric parameters and in the binding energies (ΔE) of Cu(III) intermediates may partly explain why (−)-sparteine based copper catalysts are so effective in promoting activation of aryl−chlorine bonds for cross-coupling with various nitrogen heterocycles.

3. Conclusions

In conclusion, we have shown that the easy-to-prepare dimeric copper(I) complexes with quinolizidine alkaloid (−)-sparteine are versatile catalysts for N-arylation of NH−heterocycles with variety of structurally divergent aryl halides including activated aryl chloride substrates. This protocol is very cost-effective because (−)-sparteine is readily available at a reasonable price. The DFT studies (gas phase) with the higher valent Cu(III) complexes containing (−)-sparteine provide insights into sterically demanding sparteine ligand framework in promoting activation of aryl−chlorine bonds for N-arylation with imidazole.

4. Experimental

4.1. General experimental procedure for direct N-arylation of NH−heterocycles using bis(μ-iodo)bis((−)-sparteine)-dicopper(I)

A mixture of aryl iodide or aryl bromide substrates (1 mmol), imidazole (1.2 mmol), potassium carbonate (2 mmol), and dimeric copper(I) catalyst (0.05 mmol) (5 mol % relative to substrate) was stirred in DMSO (5 mL) at 115 °C under nitrogen atmosphere (for aryl chloride substrates, the reaction temperature was maintained at 125 °C). The progress of the coupling reaction was monitored by TLC studies. After the completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (3×50 mL). The combined organic extracts were dried over anhydrous Na_2SO_4 and filtered. Solvent was evaporated under reduced pressure to give the crude product which was purified by column chromatography on silica gel (hexane/ethyl acetate) to afford the product in good yields (see Table 2). All compounds were characterized by both ^{1}H NMR and EIMS spectroscopies, and compared with those of data reported in the literature.[8a,9l,15,24a,41] Analytical data for compounds listed in Table 2 are given below.

4.1.1. 1-Phenyl-1H-imidazole (Table 2, entries 1 and 6)

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.83 (br s, 1H), 7.50−7.30 (m, 5H), 7.25 (br s, 1H), 7.18 (br s, 1H); EIMS: *m*/*z*=144.

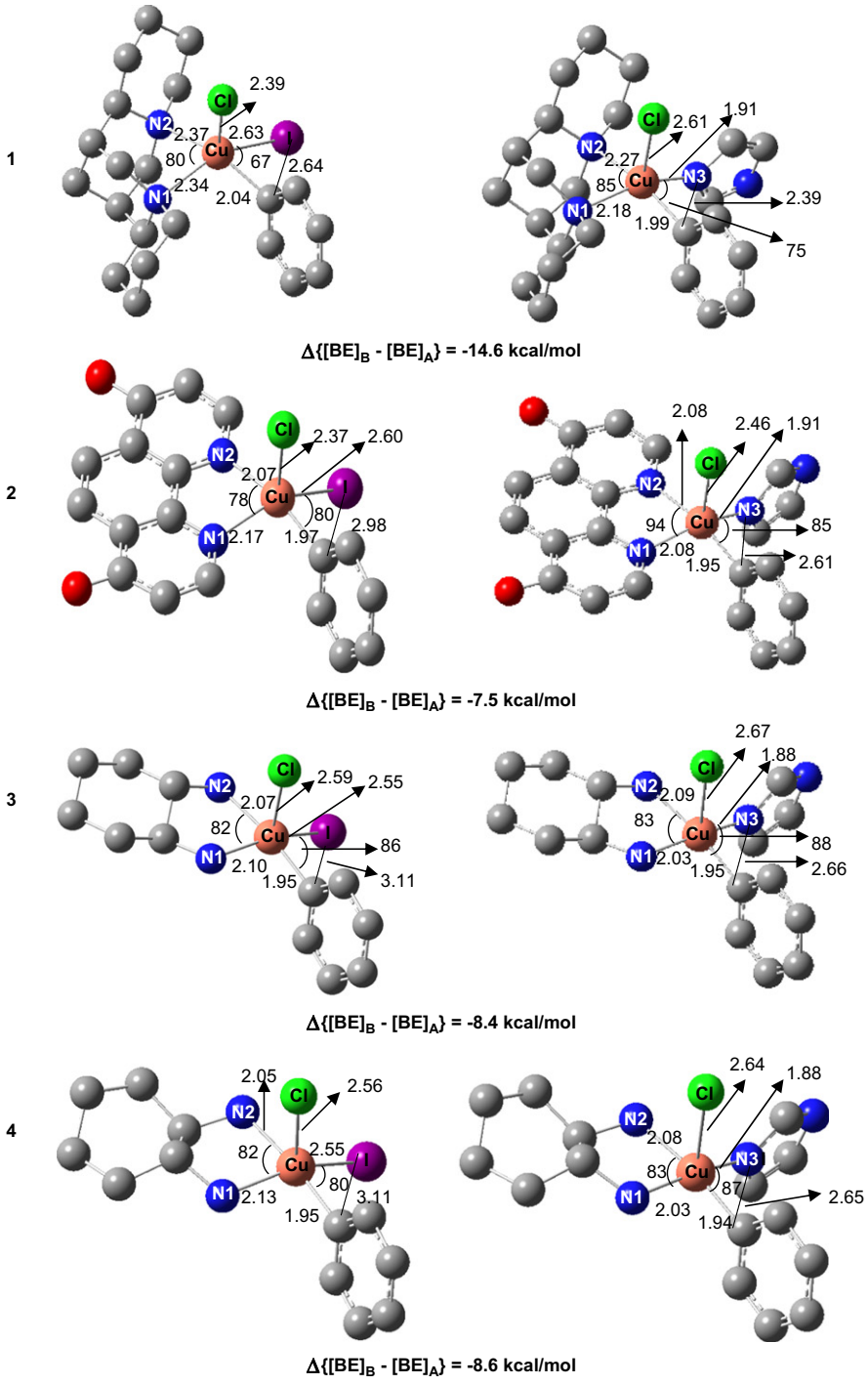


Figure 2. 3D representations of DFT optimized geometries (with BLYP functionals) along with important geometric parameters for Cu(III) intermediates (**A** and **B**) derived from (1) (−)-sparteine, (2) 4,7-dihydroxy-1,10-phenanthroline, (3) *trans*-1,2-cyclohexyldiamine (*chair*), and (4) *trans*-1,2-cyclohexyldiamine (*boat*) ligands. Hydrogen atoms are omitted for clarity. See Supplementary data for PW91 functional optimized DFT geometries.

4.1.2. 1-Phenyl-1H-pyrazole (Table 2, entry 7)

^{1}H NMR (300 MHz, $CDCl_3$): δ 6.43 (t, 1H, J=2.4 Hz), 7.24–7.28 (m, 1H), 7.39–7.45 (m, 2H), 7.68–7.74 (m, 3H), 7.88 (d, 1H, J=2.4 Hz); EIMS: m/z=144.

4.1.3. 1-(4-Methoxyphenyl)-1H-imidazole (Table 2, entries 2 and 8)

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.71 (br s, 1H), 7.28 (d, 2H, J=9.0 Hz), 7.15 (br s, 1H), 7.11 (br s, 1H), 6.94 (d, 2H, J=9.0 Hz), 3.83 (s, 3H); EIMS: m/z=174.

4.1.4. 1-(4-Methoxyphenyl)-1H-benzimidazole (Table 2, entries 3 and 9)

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.06 (s, 1H), 7.85–7.89 (m, 1H), 7.40–7.48 (m, 3H), 7.29–7.36 (m, 2H), 7.06–7.10 (m, 2H), 3.90 (s, 3H); EIMS: m/z=224.

4.1.5. 1-(4-Methoxyphenyl)-1H-pyrazole (Table 2, entries 4 and 10)

^{1}H NMR (300 MHz, DMSO-d_6): δ 8.35 (m, 1H), 7.72–7.79 (m, 2H), 7.70 (m, 1H), 7.04 (m, 2H), 6.49 (m, 1H), 3.78 (s, 3H); EIMS: *m*/*z*=174.

4.1.6. 1-(3-Methoxyphenyl)-1H-imidazole (Table 2, entry 11)

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.86 (s, 1H), 7.12–7.52 (m, 6H), 3.81 (s, 3H); EIMS: *m*/*z*=174.

4.1.7. 1-(4-Methylphenyl)-1H-imidazole (Table 2, entry 12)

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.76 (s, 1H), 7.24 (m, 4H), 7.19 (br s, 1H), 7.13 (br s, 1H), 2.39 (s, 3H); EIMS: *m*/*z*=158.

4.1.8. 1-(2-Methoxyphenyl)-1H-imidazole (Table 2, entries 5 and 13)

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.88 (br s, 1H), 7.34 (t, 1H, *J*=7.6 Hz), 7.28 (d, 1H, *J*=7.6 Hz), 7.20 (br s, 1H), 7.02–7.07 (m, 2H), 6.90 (br s, 1H), 3.84 (s, 3H); EIMS: *m*/*z*=174.

4.1.9. 1-(4-Acetyl-1-phenyl)-1H-imidazole (Table 2, entries 14 and 30)

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.95–8.15 (m, 3H), 7.45–7.58 (d, 2H), 7.15–7.40 (m, 2H), 2.64 (s, 3H); EIMS: *m*/*z*=186.

4.1.10. 1-(4-Acetyl-1-phenyl)-1H-benzimidazole (Table 2, entries 15 and 31)

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.25–8.35 (d, 2H), 7.80–7.90 (m, 1H), 7.55–7.71 (m, 3H), 7.30–7.40 (m, 3H), 2.65 (s, 3H); EIMS: *m*/*z*=236.

4.1.11. 1-(4-Formylphenyl)-1H-imidazole (Table 2, entries 16 and 32)

^{1}H NMR (300 MHz, $CDCl_3$): δ 10.02 (s, 1H), 8.00 (d, 2H, *J*=8.3 Hz), 7.93 (br s, 1H), 7.57 (d, 2H, *J*=8.3 Hz), 7.33 (br s, 1H), 7.21 (br s, 1H); EIMS: *m*/*z*=172.

4.1.12. 1-(4-Formylphenyl)-1H-pyrazole (Table 2, entries 17 and 33)

^{1}H NMR (300 MHz, $CDCl_3$): δ 10.05 (s, 1H), 8.09–7.90 (m, 5H), 7.93 (br s, 1H), 7.78 (m, 1H), 6.55 (m, 1H); EIMS: *m*/*z*=172.

4.1.13. 1-(4-Formylphenyl)-1H-benzimidazole (Table 2, entries 18 and 34)

^{1}H NMR (300 MHz, $CDCl_3$): δ 10.00 (s, 1H), 8.19 (s, 1H), 7.98–8.02 (m, 3H), 7.68–7.75 (m, 2H), 7.59–7.62 (m, 1H), 7.41–7.43 (m, 2H); EIMS: *m*/*z*=222.

4.1.14. 1-(4-Nitrophenyl)-1H-imidazole (Table 2, entries 19 and 23)

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.37 (d, 2H, *J*=9.0 Hz), 7.93 (br s, 1H), 7.58 (d, 2H, *J*=9.0 Hz), 7.32 (br s, 1H), 7.24 (br s, 1H); EIMS: *m*/*z*=189.

4.1.15. 1-(4-Nitrophenyl)-1H-benzimidazole (Table 2, entries 20 and 22)

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.47 (d, 2H, *J*=9.0 Hz), 8.12 (br s, 1H), 7.88 (m, 1H), 7.74 (d, 2H, *J*=9.0 Hz), 7.56 (m, 1H), 7.41–7.33 (m, 2H); EIMS: *m*/*z*=239.

4.1.16. 1-(4-Cyanophenyl)-1H-imidazole (Table 1, entries 21 and 25)

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.90 (br s, 1H), 7.79 (d, 2H, *J*=8.3 Hz), 7.53 (d, 2H, *J*=8.3 Hz), 7.29 (br s, 1H), 7.22 (br s, 1H); EIMS: *m*/*z*=169.

4.1.17. 1-(2-Nitrophenyl)-1H-imidazole (Table 1, entry 24)

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.98 (dd, 1H, *J*=1.5, 8.3 Hz), 7.7 (dt, 1H, *J*=1.5, 7.5 Hz), 7.64–7.57 (m, 2H), 7.47 (dd, 1H, *J*=1.5, 7.5 Hz), 7.18 (br s, 1H), 7.03 (br s, 1H); EIMS: *m*/*z*=189.

4.1.18. 1-(4-Cyano-1-phenyl)-1H-benzimidazole (Table 2, entry 26)

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38–7.42 (m, 2H), 7.56–7.61 (m, 1H), 7.68–7.71 (m, 2H), 7.89–7.93 (m, 3H), 8.16 (s, 1H); EIMS: *m*/*z*=219.

4.1.19. 1-(2-Cyanophenyl)-1H-imidazole (Table 2, entry 27)

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.57–7.32 (m, 3H), 7.27–7.12 (m, 2H), 7.02 (br s, 1H), 6.80 (br s, 1H); EIMS: *m*/*z*=169.

4.1.20. 1-(2-Cyano-1-phenyl)-1H-benzimidazole (Table 2, entry 28)

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36–7.41 (m, 3H), 7.63 (t, 2H, *J*=7.22 Hz), 7.83 (td, 1H, *J*=7.94, 1.48 Hz), 7.90–7.94 (m, 2H), 8.19 (s, 1H); EIMS: *m*/*z*=219.

4.1.21. 1-(4-Trifluoromethylphenyl)-1H-imidazole (Table 2, entry 29)

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.84 (br s, 1H), 7.69 (d, 2H, *J*=8.91 Hz), 7.46 (d, 2H, *J*=8.91 Hz), 7.23 (br s, 1H), 7.14 (br s, 1H); EIMS: *m*/*z*=212.

Acknowledgements

G.G.K., K.L.P., V.S., G.K.C. thank both IICT and CSIR (India) for research fellowship. H.M. also thanks CSIR for financial support under grant CMM-0005.

Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2007.12.050.

References and notes

1. (a) Quan, M. L.; Lam, P. Y. S.; Han, Q.; Pinto, D. J. P.; He, M. Y.; Li, R.; Ellis, C. D.; Clark, C. G.; Teleha, C. A.; Sun, J. H.; Alexander, R. S.; Bai, S.; Luettgen, J. M.; Knabb, R. M.; Wong, P. C.; Wexler, P. R. R.

J. Med. Chem. **2005**, *48*, 1729; (b) Dyck, B.; Goodfellow, V. S.; Phillips, T.; Grey, J.; Haddach, M.; Rowbottom, M.; Naeve, G. S.; Brown, B.; Saunders, J. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 1151; (c) Craig, P. N. *Comprehensive Medicinal Chemistry*; Drayton, C. J., Ed.; Pergamon: New York, NY, 1991; Vol. 8.

2. The palladium based catalysts have also been shown to be useful for N-arylation of imidazoles, however, the lack of generality of this reaction makes this protocol very limited in scope. For recent references, see: (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, U.; Ganzer, D. *Synlett* **2003**, 2428; (d) Anderson, K. W.; Rachel, E. T.; Ikawa, T.; Altman, R. A.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2006**, *45*, 6523; (e) Wolfe, J. P.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **1999**, *38*, 2413; (f) Jiang, L.; Buchwald, S. L. Palladium-Catalyzed Aromatic Carbon–Nitrogen Bond Formation. In *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed.; de Meijere, A., Diederich, F., Eds.; Wiley-VCH: Weinheim, 2004; pp 699–760.
3. Kiyomori, A.; Marcoux, J. F.; Buchwald, S. L. *Tetrahedron Lett.* **1999**, *40*, 2657.
4. (a) Klapars, A.; Antilla, J. C.; Huang, X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2001**, *123*, 7727; (b) Antilla, J. C.; Klapars, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 11684; (c) Klapars, A.; Huang, X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 7421; (d) Antilla, J. C.; Baskin, J. M.; Barder, T. E.; Buchwald, S. L. *J. Org. Chem.* **2004**, *69*, 5578; (e) Martina, W.; Klapars, A.; Buchwald, S. L. *Org. Lett.* **2001**, *3*, 3803; (f) Altman, R. A.; Buchwald, S. L. *Org. Lett.* **2006**, *8*, 2779; (g) Altman, R. A.; Koval, E. D.; Buchwald, S. L. *J. Org. Chem.* **2007**, *72*, 6190; (h) Kwong, F. Y.; Klapars, A.; Buchwald, S. L. *Org. Lett.* **2002**, *4*, 581; (i) Kwong, F. Y.; Buchwald, S. L. *Org. Lett.* **2003**, *5*, 793; (j) Klapars, A.; Parris, S.; Anderson, K. W.; Buchwald, S. L. *J. Am. Chem. Soc.* **2004**, *126*, 3529.
5. For reviews, see: (a) Okano, K.; Tokuyama, H.; Fukuyama, T. *Org. Lett.* **2003**, *5*, 4987; (b) Han, C.; Shen, R.; Su, S.; Porco, J. A., Jr. *Org. Lett.* **2004**, *6*, 27; (c) Buck, E.; Song, Z. J.; Tschaen, D.; Dormer, P. G.; Volante, R. P.; Reider, P. J. *Org. Lett.* **2002**, *4*, 1623.
6. (a) Gujadhur, R. K.; Bates, C. G.; Venkataraman, D. *Org. Lett.* **2001**, *3*, 4315; (b) van Allen, D.; Venkataraman, D. *J. Org. Chem.* **2003**, *68*, 4590; (c) Bates, C. G.; Gujadhur, R. K.; Venkataraman, D. *Org. Lett.* **2002**, *4*, 2803; (d) Gujadhur, R.; Venkataraman, D. *Synth. Commun.* **2001**, *31*, 2865; (e) Gujadhur, R.; Venkataraman, D.; Kintigh, J. T. *Tetrahedron Lett.* **2001**, *42*, 4791; (f) Gujadhur, R. K.; Venkataraman, D. *Tetrahedron Lett.* **2003**, *44*, 81.
7. Kuil, M.; Bekedam, L.; Visser, G. M.; van den Hoogenband, A.; Terpstra, J. W.; Kamer, P. C. J.; Kamer van Leeuwen, P. W. N. M.; van Strijdonck, G. P. F. *Tetrahedron Lett.* **2005**, *46*, 2405.
8. (a) Cristau, H.-J.; Cellier, P. P.; Spindler, J.-F.; Taillefer, M. *Eur. J. Org. Chem.* **2004**, 695; (b) Cristau, H.-J.; Cellier, P. P.; Spindler, J.-F.; Taillefer, M. *Chem.—Eur. J.* **2004**, *10*, 5607.
9. (a) Ma, D.; Zhang, Y.; Yao, J.; Wu, S.; Tao, F. *J. Am. Chem. Soc.* **1998**, *120*, 12459; (b) Ma, D.; Xia, C. *Org. Lett.* **2001**, *3*, 2583; (c) Ma, D.; Cai, Q.; Zhang. *Org. Lett.* **2003**, *5*, 2453; (d) Ma, D.; Cai, Q. *Org. Lett.* **2003**, *5*, 3799; (e) Ma, D.; Cai, Q. *Synlett* **2004**, 128; (f) Pan, X.; Cai, Q.; Ma, D. *Org. Lett.* **2004**, *6*, 1809; (g) Zhu, W.; Ma, D. *Chem. Commun.* **2004**, 888; (h) Ma, D.; Liu, F. *Chem. Commun.* **2004**, 1934; (i) Cai, Q.; Zhu, W.; Zhang, H.; Zhang, Y.; Ma, D. *Synthesis* **2005**, 496; (j) Deng, W.; Wang, Y.; Zou, W.; Liu, L.; Guo, Q. *Tetrahedron Lett.* **2004**, *45*, 2311; (k) Deng, W.; Zou, Y.; Wang, Y. F.; Liu, F.; Guo, Q. X. *Synlett* **2004**, 1254; (l) Ma, D.; Cai, Q.; Zhang, H. *J. Org. Chem.* **2005**, *70*, 5164.
10. Alcalde, E.; Dinarès, I.; Rodríguez, S.; Garcia de Miguel, C. *Eur. J. Org. Chem.* **2005**, 1637.
11. Liu, L.; Frohn, M.; Xi, N.; Celia, D.; Randy, H.; Reider, P. J. *J. Org. Chem.* **2005**, *70*, 10135.
12. Jerphagnon, T.; van Klink, G. P. M.; de Vries, J. G.; van Koten, G. *Org. Lett.* **2005**, *7*, 5241.
13. Xu, L.; Zhu, D.; Wang, R.; Wan, B. *Tetrahedron* **2005**, *61*, 6553.
14. Guo, X.; Rao, H.; Fu, H.; Jiang, Y.; Zhao, Y. *Adv. Synth. Catal.* **2007**, *348*, 2197.
15. Zhu, L.; Cheng, L.; Zhang, Y.; Xie, R.; You, J. *J. Org. Chem.* **2007**, *72*, 2737.
16. Selected nitrogen ligands' costs obtained from 2007–2008 Sigma–Aldrich Catalog (India-Edition): (1) 4,7-dihydroxy-1,10-phenanthroline—1 g—97.6 USD; (2) 1,10-phenanthroline—100 g—177.4 USD; (3) 4,7-dimethoxy-1,10-phenanthroline—1 g—472.4 USD; (4) (−)-sparteine—100 mL—164.4 USD; (5) L-proline—100 g—233.4 USD (USD=US $).
17. Maheswaran, H.; Prasanth, K. L.; Krishna, G. G.; Ravikumar, K.; Sridhar, B.; Kantam, M. L. *Chem. Commun.* **2006**, 4066.
18. (a) Golub, G.; Cohen, H.; Paoletti, P.; Bencini, A.; Messori, L.; Bertini, I.; Meyerstein, D. *J. Am. Chem. Soc.* **1995**, *117*, 8353; (b) Meyerstein, D. *Coord. Chem. Rev.* **1999**, *185–186*, 141; (c) Bernhardt, P. V. *J. Am. Chem. Soc.* **1997**, *119*, 771; (d) Bernhardt, P. V. *Inorg. Chem.* **2001**, *40*, 1086.
19. Copper(I) ion shows diversity in coordination geometries, and is capable of attaining linear, triangular planar, or tetrahedral structures. For a comprehensive review on haloamine–copper(I) complexes, see: Caulton, K. G.; Davies, G.; Holt, E. M. *Polyhedron* **1990**, *9*, 2319.
20. Johansson, A.; Vestergren, M.; Håkansson, M.; Gustafsson, B.; Jagner, S. *New J. Chem.* **2004**, *28*, 1000.
21. (a) Venkatraman and co-workers have shown preformed Cu(I) phosphine complexes of general formula $CuXL(Ph_3P)_2$ L=phenanthroline or its derivative Neocuproine are effective for C–C, C–O, C–N, and C–X cross-coupling reactions; see Refs. 5a,b. Hitherto, these preformed catalysts have not been reported for C–N cross-coupling with azoles. (b) For amination and amidation of aryl iodides with preformed copper(I)–phenanthroline complexes, see: Moriwaki, K.; Satoh, K.; Takada, M.; Ishino, Y.; Ohno, T. *Tetrahedron Lett.* **2005**, *46*, 7559.
22. Alami, M.; Amatore, C.; Bensalem, S.; Abdelharim, C.-B.; Jutand, A. *Eur. J. Inorg. Chem.* **2001**, 2675.
23. Espino, G.; Kurbangalieva, A.; Brown, J. M. *Chem. Commun.* **2007**, 1742.
24. (a) Choudary, B. M.; Sridhar, C.; Kantam, M. L.; Venkanna, G. T.; Sreedhar, B. *J. Am. Chem. Soc.* **2005**, *127*, 9948; (b) Son, S. U.; Park, I. K.; Park, J.; Hyeon, T. *Chem. Commun.* **2004**, 778.
25. (a) Weingarten, H. *J. Org. Chem.* **1964**, *29*, 3624; (b) Cohen, T.; Wood, J.; Dietz, A. G. *Tetrahedron Lett.* **1974**, 3555; (c) Cohen, T.; Cristea, I. *J. Org. Chem.* **1975**, *40*, 3649; (d) Cohen, T.; Cristea, I. *J. Am. Chem. Soc.* **1976**, *98*, 748; (e) Paine, A. J. *J. Am. Chem. Soc.* **1987**, *109*, 1496; (f) Bowman, W. R.; Heaney, H.; Smith, P. H. G. *Tetrahedron Lett.* **1984**, *25*, 5821; (g) Allen, D. V. Methodology and Mechanism: Reinvestigating the Ullmann reaction. Ph.D. Dissertation, Submitted to The Graduate School of University of Massachussetts, Amherst, 2004.
26. Venkataraman and co-workers have proposed an alternate σ-bond metathesis mechanism to account for cross-coupling reactions with preformed copper(I) catalysts (1,10-phenanthroline)-$Cu(Ph_3P)_3X$ and (neocuproine)$Cu(Ph_3P)_3X$; where X=I, Br, or Cl. See Ref. 25g for more details.
27. (a) Diaddario, L. L.; Robinson, W. R.; Margerum, D. L. *Inorg. Chem.* **1983**, *22*, 1021; (b) Wasbotten, I. H.; Wondimageng, T.; Ghosh, A. *J. Am. Chem. Soc.* **2002**, *124*, 8104; (c) Furuta, H.; Maeda, H.; Osuka, A. *J. Am. Chem. Soc.* **2000**, *122*, 803; (d) Stepien, M.; Latos-Grazynski, L. *Chem.—Eur. J.* **2001**, *7*, 5113; (e) Willert-Porada, M. A.; Burton, D. J.; Baenziger, N. C. *J. Chem. Soc., Chem. Commun.* **1989**, 1633; (f) Naumann, D.; Roy, T.; Tebbe, K. F.; Crump, W. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1482; (g) Eujen, R.; Hoge, B.; Brauer, D. J. *J. Organomet. Chem.* **1996**, *519*, 7; (h) Carsten, K.; Thorsten, G.; Eckhard, B.; Thomas, W.; Wolfram, M.-K.; Karl, W. *Angew. Chem., Int. Ed.* **1999**, *39*, 359.
28. Bertz, S. H.; Cope, S.; Murphy, M.; Ogle, C. A.; Taylor, B. J. *J. Am. Chem. Soc.* **2007**, *129*, 7208.
29. (a) Mirica, L. M.; Xavier, O.; Stack, T. D. P. *Chem. Rev.* **2004**, *104*, 1013; (b) Ribas, X.; Jackson, D. A.; Donnadieu, B.; Mahia, J.; Parella, T.; Xifra, R.; Hedman, B.; Hodgson, K. O.; Llobet, A.; Stack, T. D. P. *Angew. Chem., Int. Ed.* **2002**, *41*, 2991; (c) Henson, M. J.; Mukherjee, P.; Root, D. E.; Stack, T. D. P.; Solomon, E. I. *J. Am. Chem. Soc.* **1999**, *121*, 10332; (d) Cole, A. P.; Mahadevan, V.; Mirica, L. M.; Ottenwaelder, X.; Stack, T. D. P. *Inorg. Chem.* **2005**, *44*, 7345; (e) Viswanath, M.; DuBois, J. L.; Hedman, B.; Hodgson, K. O.; Stack, T. D. P. *J. Am. Chem. Soc.* **1999**, *121*, 5583; (f) Mahadevan, V.; Hou, Z.; Cole, A. P.; Root, D. E.; Lal, T. K.; Solomon, E. I.; Stack, T. D. P. *J. Am. Chem. Soc.* **1997**, *119*, 11996; (g) For (−)-sparteine derived μ-dioxo Cu(III) complexes with solution charge transfer (CT) energies that are characteristic of square-pyramidal geometry at copper, see: Funahashi, Y.; Nakaya, K.; Hirota, S.; Yamauchi, O. *Chem. Lett.* **2000**, 1172.

30. (a) Golubkov, G.; Bendix, J.; Gray, H. B.; Mahammed, A.; Goldberg, I.; DiBilio, A. J.; Gross, Z. *Angew. Chem., Int. Ed.* **2001**, *40*, 2132; (b) Gryko, D. T. *Eur. J. Org. Chem.* **2002**, 1735; (c) Gryko, D. T.; Fox, J. P.; Goldberg, D. P. *J. Porphyrins Phthalocyanines* **2004**, *8*, 1091; (d) Nardis, S.; Monti, D.; Paolesse, R. *Mini-Rev. Org. Chem.* **2005**, *2*, 355; (e) Edwards, N. Y.; Eikey, R. A.; Loring, M. I.; Abu-Omar, M. M. *Inorg. Chem.* **2005**, *44*, 3700; (f) Eikey, R. A.; Khan, S. I.; Abu-Omar, M. M. *Angew. Chem., Int. Ed.* **2002**, *41*, 3592; (g) Golubkov, G.; Gross, Z. *J. Am. Chem. Soc.* **2005**, *127*, 3258.
31. Bröring, M.; Hell, C.; Brandt, C. D. *Chem. Commun.* **2007**, 1861.
32. (a) Xifra, R.; Ribas, X.; Llobet, A.; Poater, A.; Duran, M.; Sol, M.; Stack, T. D. P.; Benet-Buchholz, J.; Donnadieu, B.; Mahia, J.; Parella, T. *Chem.—Eur. J.* **2005**, *11*, 5146; (b) See CCDC-261435 at Cambridge Crystallographic Data Centre for the X-ray structure of triazamacrocycle ligand derived square-pyramidal $[Cu^{III}(L)Cl]^{+}[ClO_4]^{-}$ complexes.
33. In contrast to square-pyramidal Cu(III) complexes, the square-planar Cu(III) complexes show significant cathodic shifts in $E_{1/2}$ values when the substituents on the phenyl ring is electron-withdrawing (example, NO_2), which corresponds to large destabilization of the Cu(III) center: see Ref. 32a for further details.
34. Kozuch, S.; Shaik, S.; Jutand, A.; Amatore, C. *Chem.—Eur. J.* **2004**, *10*, 3072.
35. Yamashita, M.; Takamiya, I.; Jin, K.; Nozaki, K. *J. Organomet. Chem.* **2006**, *691*, 3189.
36. (a) Wolfe, J. P.; Seble, W.; Marcoux, J.-F.; Buchwald, S. L. *Acc. Chem. Res.* **1998**, *35*, 805; (b) Timothy, E. B.; Mark, R. B.; Buchwald, S. L. *Organometallics* **2007**, *26*, 2183.
37. ADF2006.01, SCM, Theoretical Chemistry, Vrije Universiteit, Amsterdam, The Netherlands; see Supplementary data for complete references.
38. (a) Yang, X.; Hall, M. B. *J. Am. Chem. Soc.* **2007**, *129*, 1560 also see: (b) Anthony, J. D.; Green, J. C.; McGrady, G. S.; Neil, M.; Parkin, R. P. G. *J. Chem. Soc., Dalton Trans.* **2000**, 21.
39. Instead of 4,7-dimethoxy-1,10-phenanthroline ligand, its unmethylated analog 4,7-dihydroxy-1,10-phenanthroline was employed for computational studies for convenience.
40. In solution, preferential formation of dimeric $[Cu_2I_2(1,10\text{-phenanthroline})_2]$ complex with Cu_2I_2 core has been reported, see: (a) Healy, P. C.; Pakawatchai, C.; White, A. H. *J. Chem. Soc., Dalton Trans.* **1985**, 2531; (b) Yu, J.-H.; Lü, Z.-L.; Xu, J.-Q.; Bie, H.-Y.; Lu, J.; Zhang, X. *New J. Chem.* **2004**, *28*, 940; (c) Skelton, B. W.; Waters, A. F.; White, A. H. *Aust. J. Chem.* **1991**, *44*, 1207.
41. (a) Collman, J. P.; Zhong, M. *Org. Lett.* **2000**, *2*, 1233; (b) Nishiura, K.; Urawa, Y.; Sodab, S. *Adv. Synth. Catal.* **2004**, *346*, 1679.