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First Copper(I) Ferrocenyltetraphosphine Complexes: Possible Involvement in Sonogashira Cross-Coupling Reaction?

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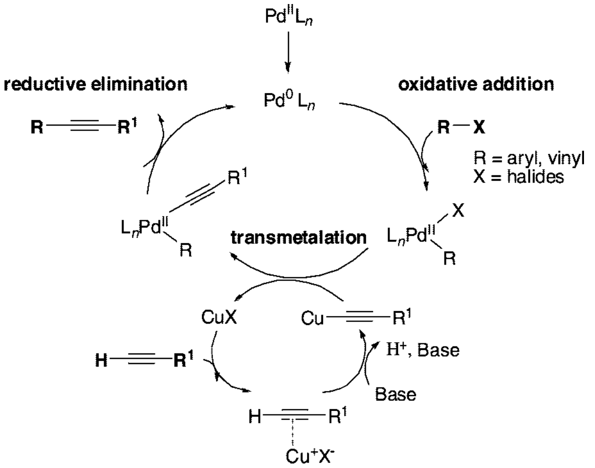
Preparation and characterization of the first examples of copper(I) ferrocenylpolyphosphine complexes are reported. The molecular structure of complex {P,P′,P″-[1,1′,2,2′-tetrakis(diphenylphosphino)-4,4′-di-*tert*-butylferrocene]iodocopper(I)} (**1**) was solved by X-ray diffraction studies, and its fluxional behavior in solution was investigated by VT-^{31}P NMR; both revealed a net triligated coordination preference of the ferrocenyl tetraphosphine Fc(P)$_4$^{t}Bu with copper. The tetradentate ligand is an active auxiliary in Sonogashira alkynylation; therefore the general question of copper as a competitive coordination partner in the Pd/Cu-catalyzed Sonogashira reaction was raised and discussed. Electronically neutral, activated, and deactivated aryl bromides were employed for coupling with phenylacetylene with various [(Pd)/(Cu)/(tetraphosphine)] systems. The catalytic investigations shown that 1 mol % of complex **1** in combination with palladium is far more effective and selective for Sonogashira coupling than 5 mol % of CuI and palladium in the coupling to phenylacetylene of the deactivated aryl bromide 4-bromoanisole. This system efficiently avoids the concurrent and deleterious consumption of phenylacetylene by formation of diyne or enynes. To our knowledge, this is the first time that this kind of high selectivity is induced in Sonogashira alkynylation by initial ligand complexation to copper instead of palladium. These results demonstrate that coordination of Cu halide cocatalyst is a factor that should no longer be neglected in mechanistic and applied studies of the Sonogashira reaction.

Introduction

The palladium/copper-cocatalyzed alkynylation of aryl and vinyl halides, usually identified as Sonogashira−Tohda−Hagihara cross-coupling, is among the most widely employed methodologies to yield valuable (aryl)alkynes.[1] The exact mechanism of the homogeneous copper-cocatalyzed Sonogashira reaction is not yet well-understood and is generally supposed to take place through two independent catalytic cycles, as depicted in Scheme 1.

While the first cycle involving palladium is classical from C−C cross-coupling formation, the second cycle generally involving copper(I) iodide is poorly known.[2] The base that can be either organic (amines) or inorganic (carbonates) is believed to assist the copper acetylide formation, with the help of a π-alkyne copper complex, which would make the alkyne terminal proton more acidic. The most efficient catalytic systems reported up to now involve a myriad of different ligands for which the coordination properties are commonly reported with palladium (L_n in Scheme 1).[1] Curiously, to the best of our knowledge, the few mechanistic studies around Sonogashira cross-coupling[2] have neglected the possible interference of copper as transition metal and the potential concurrent formation of CuXL$_n$-type species, which appears to us an interesting parameter that could bring helpful information.[3] Therefore, the issue of the coordination of useful ligands to copper might be examined in the future on a more regular basis.

Scheme 1. Catalytic Cycles Proposed for Pd/Cu-Cocatalyzed Sonogashira Alkynylation



For our part, we have recently disclosed that ferrocenyl polyphosphines can be very efficient as ligands in Sonogashira alkynylations (Scheme 2): the triphosphine ligand Fc(P)$_2$^{t}Bu-(P^{i}Pr) allows aryl alkynylation from organic bromides and chlorides at 10^{-1} to 10^{-4} mol % catalyst loading with TONs up to 250 000;[4] with the diphosphine Fc[P(FuMe)$_2$]$_2$ a TON of

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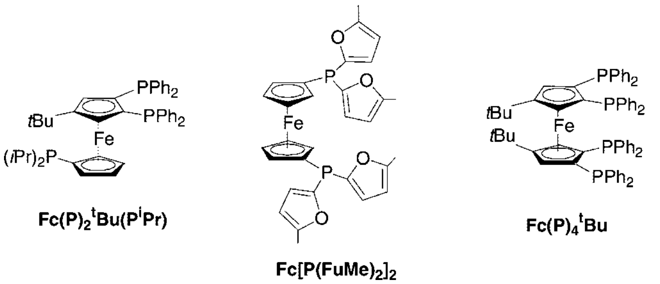
(1) Doucet, H.; Hierso, J.-C. *Angew. Chem., Int. Ed.* **2007**, *46*, 834.

(2) Chinchilla, R.; Nájera, C. *Chem. Rev.* **2007**, *107*, 874.

(3) (a) Osakada, K.; Sakata, R.; Yamamoto, T. *Organometallics* **1997**, *16*, 5354, and references therein. In this very relevant article the authors investigated intermolecular alkynyl-ligand transfer between copper(I) and Pd(II) and showed the intricate influence of PPh$_3$ and PEt$_3$ on the reaction, as well as the possible formation of large amounts of CuI(PPh$_3$)$_3$. (b) For a review see: Osakada, K.; Yamamoto, T. *Coord. Chem. Rev.* **2000**, *198*, 379.

10.1021/om700700q CCC: $40.75

Scheme 2. Ferrocenylpolyphosphine Ligands Used in C−C and C−N Bond Formation



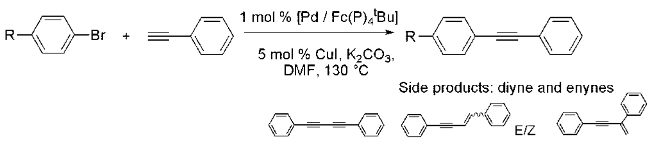
920 000—among the highest reported—was obtained in the coupling of 4-bromoacetophenone to phenylacetylene.[5]

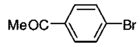
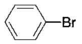
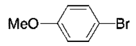
We report herein that the tetraphosphine ligand Fc(P)$_4$^{t}Bu, 1,1′,2,2′-tetrakis(diphenylphosphino)-4,4′-di-*tert*-butylferrocene, which is a very efficient auxiliary in palladium-catalyzed Suzuki and Heck reactions,[6] also provides active systems in the Sonogashira reaction in the presence of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and copper. More importantly, the coordination properties of this tetraphosphine ligand with copper halides were examined, and the X-ray characterization of the first complexes of group 11 for this class of ferrocenyl polyphosphines is reported.[7] The resulting complexes are air-stable *P*-triligated tetrahedral copper(I) species, on which X-ray diffraction studies, VT-^{31}P NMR spectroscopy, exact mass, UV, and EPR measurements were conducted. In light of the studies devoted to copper complex preparation, the likelihood and interest of copper−phosphine coordinative interference in Sonogashira cross-coupling reactions is discussed for the first time, to our knowledge, concerning this cocatalyzed reaction.

Results and Discussion

Preliminary Catalytic Experiments. The rich coordination chemistry of Fc(P)$_4$^{t}Bu toward palladium has been correlated to its performances in C−C cross-coupling catalysis.[6,8] Experimental conditions and results in Sonogashira alkynylation for the catalytic system combining the palladium(II) precursor complex $[PdCl(\eta^3\text{-}C_3H_5)]_2$ with the tetradentate ligand Fc(P)$_4$^{t}Bu are presented in Table 1. Electronically neutral, activated, and deactivated aryl bromides were coupled to phenylacetylene. The nature of the substituent on the organic halide plays an important role: indeed, in the absence of an electron-withdrawing substituent on the aryl partner, concomitant phenylacetylene dimerization (Hay−Glaser copper-catalyzed coupling and/or [Pd/Cu]-cocatalyzed alkyne dimerization to enynes) hampered a total aryl alkynylation (due to alkyne consumption; see Table 1, entries 2 and 3).[1,9]

Table 1. Sonogashira Alkynylation with Pd/Fc(P)$_4$^{t}Bu Catalytic System



Entry	Aryl bromide[a]	Yield (%)
1	 MeOC—Br	100
2	 Br	32[b]
3	 MeO—Br	20[b]

[a] Nonoptimized catalytic conditions: (alkyne:aryl) 2:1, 2 equiv of K_2CO_3, 24 h in 10 mL of DMF at 130 °C; GC average yields from two or three runs are given. [b] Phenylacetylene dimerization to enynes, as described in ref 9, is responsible for lower yields; in all runs unconverted bromobenzene (entry 2) or bromoanisole is observed (entry 3) in more than 30% yield.

Complex Preparation and Characterization. On the basis of the preliminary results obtained in Sonogashira alkynylation reactions with the system Pd/CuI/ferrocenyltetraphosphine, we started to explore several synthetic conditions to form copper coordination complexes with the tetraphosphine metalloligand Fc(P)$_4$^{t}Bu. Our first objective was to disclose the coordination preference of ferrocenylpolyphosphines toward copper halides. Additionally, the prediction of the number of copper nucleus atoms able to coordinate the ligand, as well as the final geometry of the possible coordination complexes formed, was not *a priori* evident since the coordination chemistry of polyphosphines (three or more phosphorus atoms available) toward copper is scantily developed.[10]

The first experimental conditions we tested by reacting Fc(P)$_4$^{t}Bu with 4-fold equivalent of the simple copper chloride hydrate (ratio Cu:P $\approx$ 1 is standard conditions in catalytic runs) at ambient temperature in DMF, toluene, dichloromethane, THF, methanol (in the presence or without trimethylorthoformate as dehydrating agent), and acetonitrile were unsuccessful. Under similar conditions at 50 °C in methanol and THF, ^{31}P NMR spectroscopy showed the formation of mixtures of coordination species we failed to isolate and crystallize.[11] The same phenomenon was observed by employing under analogous conditions refluxing acetonitrile as the solvent. In an attempt to make things easier, several reactions involving only 1 or 2 equivalents of copper chloride to the ligand were investigated with analogous results.[11] We then turned our attention to anhydrous copper iodide as inorganic complex precursor, this particular compound being moreover ubiquitous in Sonogashira alkynylations. Suitable conditions were finally identified for reproducible formation of copper−tetraphosphine coordination complex **1** depicted in Scheme 3. From the mixture of 4 equiv of anhydrous CuI with Fc(P)$_4$^{t}Bu in deoxygenated acetonitrile, at reflux for 3 h, a 1,1′,2-*P*-triligated copper iodide complex is obtained. The complex is isolated from solution as orange needles after a night at −18 °C; the excess of CuI cocrystallizes as white, square-shaped crystals of a polymeric inorganic copper compound, catena-[(μ^3-iodo)(acetonitrile-*N*)copper(I)].[12]

In the course of our syntheses and attempts to identify alternative coordination modes for copper, we obtained a surprising result, important to mention, regarding cyclopentadienyl−alkali metal chemistry (see below). X-ray quality single crystals of a copper(I) complex stabilized by the unexpected ligand 1,1′,2,3′-tetrakis(diphenylphosphino)-4,4′-di-*tert*-butyl-

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[4] Hierso, J.-C.; Fihri, A.; Amardeil, R.; Meunier, P.; Doucet, H.; Santelli, M.; Ivanov, V. V. *Org. Lett.* **2004**, *6*, 3473.

[5] Hierso, J.-C.; Fihri, A.; Amardeil, R.; Meunier, P.; Doucet, H.; Santelli, M. *Tetrahedron* **2005**, *61*, 9759.

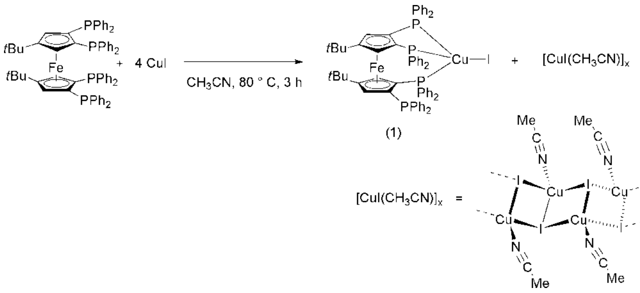
[6] Hierso, J.-C.; Fihri, A.; Amardeil, R.; Meunier, P.; Doucet, H.; Santelli, M.; Donnadieu, B. *Organometallics* **2003**, *22*, 4490.

[7] Hierso, J.-C.; Smaliy, R.; Meunier, P. *Chem. Soc. Rev.* **2007**, *36*, 1754; from the library of ferrocenyl polyphosphine ligands we developed, only coordination complexes of groups 6 to 10 were reported up to now.

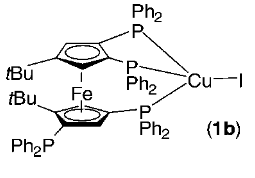
[8] Hierso, J.-C.; Fihri, A.; Ivanov, V. V.; Hanquet, B.; Pirio, N.; Donnadieu, B.; Rebière, B.; Amardeil, R.; Meunier, P. *J. Am. Chem. Soc.* **2004**, *126*, 11077.

[9] Batanov, A. S.; Collings, J. C.; Fairlamb, I. J. S.; Holland, J. P.; Howard, J. A. K.; Lin, Z.; Marder, T. B.; Parsons, A. C.; Ward, R. M.; Zhu, J. *J. Org. Chem.* **2005**, *70*, 703, and references therein. The nature of the copper species possibly involved in alkyne dimerization is also a very interesting issue.

Scheme 3. Copper Coordination Chemistry of Ferrocenyltetraphosphine Fc(P)$_4$^{t}Bu



Scheme 4. Mononuclear Copper Complex 1b



ferrocene (**1b** Scheme 4) were fortuitously formed in quite significant quantity (about 20% from ^{1}H NMR integration of Cp*H* relative to **1**). The X-ray diffraction studies were repeated on several crystals and confirmed the first analysis.

Details of the structure determinations are given in the Experimental Section. Table 2 lists crystallographic data for complexes **1** and **1b**; selected bond distances and angles are given in Table 3.

The X-ray molecular structure obtained for **1** (Figure 1) indicated that the copper(I) atom is bonded to three phosphorus atoms of the tetraphosphine in a distorted tetrahedral environment completed by a iodide [Cu−I 2.5848(14) Å]. The three metal−phosphorus bonds are substantially different [Cu−P(1) 2.310(3) Å, Cu−P(2) 2.355(2) Å, Cu−P(3) 2.273(2) Å], with a relative variation around 3.5% observed between the shortest and the longest one. In general, for the unsolvated complexes [$(PPh_3)_3CuX$] (X = halide) X-ray structural data have shown P−Cu−P and P−Cu−X angles close to the ideal tetrahedral angle of 109.5°.[13] In **1** the major deviation is observed for the closed angle P(1)−Cu−P(2) = 85.9(1)°, originating from the 1,2-*P* chelating pattern, and P−Cu−I angles lie between 116° and 121°; several molecules of acetonitrile are present in the crystals. To accommodate its *fac* tricoordination, the ferrocenyltetraphosphine ligand undergoes severe constraints worth detailing in light of the previously reported X-ray diffraction structures of the free ligand and of the mononuclear palladium complex [$PdCl_2$\{Fc(P)$_4$^{t}Bu\}].[6]

As shown in Figure 1, phosphorus P(3) almost lies in the bisecting plane of the P(1)−Ct(1)−P(2) angle [dihedral angle P(2)Ct(1)Ct(2)P(3) = −27.1(3)°]; therefore a rotation of the tetraphosphine relative to the free ligand is observed since originally phosphorus corresponding to P(2) and P(3) adopt a pseudoeclipsed conformation [equivalent dihedral angle −5.6(1)°]. In the mononuclear palladium complex [$PdCl_2$\{Fc(P)$_4$^{t}Bu\}] the mutual rotation of Cp rings was found to be much less pronounced, and thus its geometry was found closer to that of the free ligand [dihedral angle −11.2°]. In **1** the phosphorus atoms bonded to copper do not exhibit noticeable deviation from the average plane of the Cp rings; the angle between the planes encompassing the Cp rings is 5(1)°.

As shown in Table 3 the geometrical parameters regarding the copper coordination sphere for **1b** (Figure 2) are very similar to those found for **1**. The most noticeable difference in **1b** is the unexpected position of phosphorus P(4), adjacent to the ^{t}Bu group.

^{31}P\{^{1}H\} NMR spectroscopy studies were conducted on **1** in deuterated dichloromethane: at ambient temperature two signals at −23.4 and −24.6 ppm are detected (Figure 3, top); the first one is a clear singlet, whereas the second one is broader and ill-defined. Low-temperature NMR (VT, Figure 3) conducted down to −94 °C remarkably confirmed the X-ray structural studies. Upon cooling the temperature, the fluxional behavior of the copper complex is evidenced through coalescence (0 to −40 °C) and decoalescence (−60 °C) of the broader signal. Three new signals appear at −75 °C, and the occurrence of four different phosphorus from which three are in a dynamic exchange (centered at −15.1, −22.1, and −36.6 ppm) is ascertained at −94 °C. The appearance and chemical shift of the singlet are almost not modified by the variation of temperature (shift from −23.4 ppm at 27 °C to −26.7 ppm at −94 °C). The dynamic phenomenon is reversible since upon increasing the temperature again above the coalescence temperature, the spectrum exhibits again the two characteristic signals at −23.4 and −24.6 ppm. These signals are only slightly shifted downfield relative to the free ligand (multiplets at −28.6 and −32.2 ppm in $CDCl_3$).[6] The ^{1}H NMR at ambient temperature did not show excessively broad signals, so that they could be properly assigned; relative to the free ligand all the signals are shifted downfield: Cp protons give two signals at 4.25 and 4.14 ppm, the methyl groups from ^{t}Bu are detected at 0.82 ppm, and the signals corresponding to phenyl protons of the PPh_2 groups give large multiplets between 6.80 and 8.10 ppm.[11]

The VT-^{31}P NMR data evidence the lability of the copper−iodide fragment, for which the interaction with three of the four phosphorus atoms is undoubtedly observed whatever the temperature. The phosphorus corresponding to P(4) in the molecular structure in the solid state is certainly kept away from the coordination sphere of copper, even in solution at ambient temperature. The nature of the fluxional behavior visibly reveals that the three phosphorus stay bonded to copper (three signals at −94 °C, which coalesce to form one signal at rt);[14] this suggests that at higher temperature the mutual locations of phosphorus toward the copper atom (clearly nonequivalent in the solid state) are exchanged at high rate, leading to an average signal at the NMR scale rate. VT-^{31}P NMR studies on **1b** revealed a similar behavior, in which the atom P(4) give a singlet detected at −20.7 ppm and is not involved in the dynamic exchange of the three other phosphorus atoms toward CuI; they gave two broad signals at −28.3 and −22.9 ppm (with 1:2 integration ratio, respectively).[11] The ^{1}H NMR at ambient

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(10) (a) Hierso, J.-C.; Amardeil, R.; Bentabet, E.; Broussier, R.; Gautheron, B.; Meunier, P.; Kalck, P. *Coord. Chem. Rev.* **2003**, *236*, 143. A check in the Cambridge Structural Database (06/2007) revealed that X-ray diffraction studies for copper complexes with a tricoordinated polyphosphine ligand were found only for the flexible tripodal ligands 1,1,1-tris(2-diphenylphosphinomethyl)ethane and 1,1,1-tris(2-(diphenylphosphino)ethyl)amine; see for instance: (b) Garcia-Seijo, M. I.; Sevillano, P.; Gould, R. O.; Fernandez-Anca, D.; Garcia-Fernandez, M. E. *Inorg. Chim. Acta* **2003**, *353*, 206. (c) Ghilardi, C. A.; Midollini, S.; Orlandini, A. *Inorg. Chem.* **1982**, *21*, 4096.

(11) NMR spectra are available as Supporting Information.

(12) (a) Arkhireeva, T. M.; Bulychev, B. M.; Sizov, A. I.; Sokolova, T. A.; Belsky, V. K.; Soloveichik, G. L. *Inorg. Chim. Acta* **1990**, *169*, 109. (b) Healy, P. C.; Kildea, J. D.; Skelton, B. W.; White, A. H. *Aust. J. Chem.* **1989**, *42*, 79. (c) Nilsson, K.; Oskarsson, A. *Acta Chem. Scand. A* **1985**, *39*, 663. (d) Jasinski, J. P.; Rath, N. P.; Holt, E. M. *Inorg. Chim. Acta* **1985**, *97*, 91. A PovRay illustration of the staggered conformation of the catena complex is available as Supporting Information.

(13) Hanna, J. V.; Boyd, S. E.; Healy, P. C.; Bowmaker, G. A.; Skelton, B. W.; White, A. H. *Dalton Trans.* **2005**, 2547.

(14) If one phosphorus atom was alternatively released from copper coordination, at low temperature it should appear as a clear singlet.

Table 2. Crystal Data and Structure Refinement Details for 1 and 1b

	1	**1b**
formula	$C_{66}H_{62}FeCuIP_4 \cdot 3(CH_3CN)$	$C_{66}H_{62}FeCuIP_4 \cdot 3(CH_3CN)$
M	1348.49	1348.49
T, K	115(2)	115(2)
cryst syst	triclinic	triclinic
space group	$P\bar{1}$	$P\bar{1}$
a, Å	12.553(5)	11.7939(2)
b, Å	13.193(5)	15.6829(3)
c, Å	20.198(5)	18.4282(3)
α, deg	86.425(5)	91.007(1)
β, deg	76.582(5)	103.969(1)
γ, deg	79.054(5)	103.612(1)
V, Å^3	3193.9(19)	3204.8(1)
Z	2	2
F(000)	1384	1384
D_{calc}, g/cm^3	1.402	1.397
diffractometer	Nonius KappaCCD	Nonius KappaCCD
scan type	φ rot and ω scans	φ rot and ω scans
λ, Å	0.71073	0.71073
μ, mm^{-1}	1.184	1.184
cryst size, mm^3	0.30 × 0.30 × 0.175	0.45 × 0.37 × 0.25
$\sin(\theta)/\lambda_{max}$, Å^{-1}	0.65	0.65
index ranges	h −16; 16	h −15; 15
	k −14; 17	k −17; 20
	l −26; 24	l −23; 23
RC = reflns collected	17674	21864
IRC = indep RC	11 378 [R(int) = 0.0627]	14 411 [R(int) = 0.0215]
IRCGT = IRC and [$I > 2\sigma(I)$]	7174	13176
refinement method	full-matrix LS on F^2	full-matrix LS on F^2
no. of data/restraints/params	11 378/108/746	14 411/12/797
R for IRCGT	R1^a = 0.080, wR2^b = 0.164	R1^a = 0.059, wR2^b = 0.134
R for IRC	R1^a = 0.146, wR2^b = 0.199	R1^a = 0.064, wR2^b = 0.136
goodness-of-fit^c	1.067	1.218
$\Delta\rho$, max, min, e Å^{-3}	1.787 and −1.167	2.709 and −1.946

[a] $R1 = \sum(||F_o| - F_c||)/\sum|F_o|$. [b] $wR2 = [\sum w(F_o^2 - F_c^2)^2/\sum[w(F_o^2)^2]]^{1/2}$ where $w = 1/[\sigma^2(F_o^2 + (0.0552P)^2 + 28.7358P]$ for **1** and $w = 1/[\sigma^2(F_o^2 + 18.4318P]$ for **1b** where $P = (\mathrm{Max}(F_o^2,0) + 2F_c^2)/3$. [c] Goodness of fit $= [\sum w(F_o^2 - F_c^2)^2/(N_o - N_v)]^{1/2}$.

Table 3. Selected Bond Distances and Angles for Crystals of 1 (left) and 1b (right)

	Distances (Å)	
Cu−I	2.5848(14)	2.5799(6)
Cu−P(1)	2.310(3)	2.2988(12)
Cu−P(2)	2.355(2)	2.3342(12)
Cu−P(3)	2.273(2)	2.2771(11)
	Angles (deg)	
P(1)−Cu−I	120.34(6)	113.40(3)
P(2)−Cu−I	118.42(7)	125.33(4)
P(3)−Cu−I	116.57(7)	118.15(3)
P(1)−Cu−P(2)	85.93(8)	86.26(4)
P(1)−Cu−P(3)	106.92(9)	105.06(4)
P(2)−Cu−P(3)	103.81(8)	102.99(4)
P(1)−Ct(1)−Ct(2)−P(3)^a	36.2(3)	36.8(2)
P(2)−Ct(1)−Ct(2)−P(3)	−27.1(3)	−26.4(2)

[a] Ct labels refer to Cp centroids.

temperature gave four signals at 3.95, 4.09, 4.47, and 4.58 ppm for Cp protons, the methyl groups from ^{t}Bu are detected at 0.80 ppm, and the signals corresponding to phenyl protons of the PPh_2 groups give signals between 6.0 and 8.25 ppm.[11]

As mentioned above, the formation of **1b** and especially of its related ligand 1,1′,2,3′-tetrakis(diphenylphosphino)-4,4′-di-*tert*-butylferrocene was unanticipated. We examined therefore more carefully the pool of ligands we had routinely employed, and ^{31}P NMR spectroscopy confirmed the formation, in addition to $Fc(P)_4{}^t$Bu, of this new tetraphosphine.[11] The reported three-step synthesis of $Fc(P)_4{}^t$Bu from the cyclopentadienyl (Cp) lithium derivative ^{t}BuCpLi has been initially optimized to quantitatively induce the successive phosphorylations of the Cp ring in adjacent positions, i.e., in β-position from the hindered ^{t}Bu group (Scheme 5).[15]

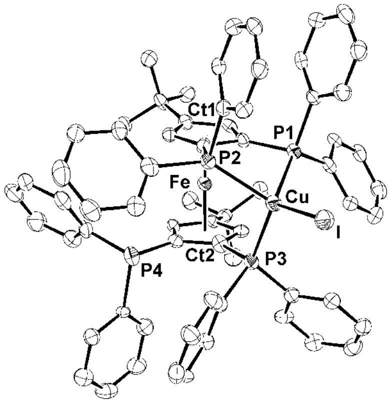

Figure 1. View of the molecular structure of copper complex **1**. Hydrogen atoms and solvate molecules are omitted for clarity. Thermal ellipsoids have been drawn at the 50% probability level.

Thus, in **1b** the position of a PPh_2 group adjacent to the ^{t}Bu group was to us rather enigmatic. A more accurate examination of synthetic conditions led to a plausible explanation (illustrated in Scheme 6) for the formation of the 1,1′,2,3′-tetrakis(diphenylphosphino)-4,4′-di-*tert*-butylferrocene as a byproduct, under certain conditions. It has been previously observed in the alkali-metal chemistry of substituted phosphino-cyclopentadiene spe-

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(15) (a) Broussier, R.; Bentabet, E.; Mellet, P.; Blacque, O.; Boyer, P.; Kubicki, M. M.; Gautheron, B. *J. Organomet. Chem.* **2000**, *598*, 365. (b) Broussier, R.; Bentabet, E.; Amardeil, R.; Richard, P.; Meunier, P.; Kalck, P.; Gautheron, B. *J. Organomet. Chem.* **2001**, *637–639*, 126.

(16) Broussier, R.; Ninoreille, S.; Legrand, C.; Gautheron, B. *J. Organomet. Chem.* **1997**, *532*, 55.

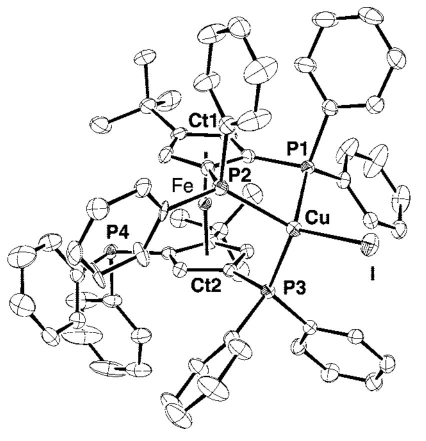


Figure 2. View of the molecular structure of copper complex **1b**. Hydrogen atoms and solvate molecules are omitted for clarity. Thermal ellipsoids have been drawn at the 50% probability level.

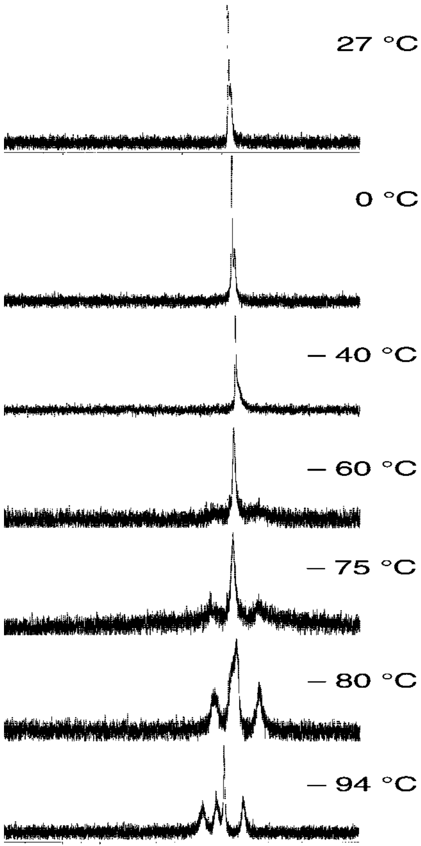
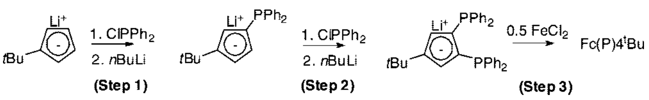


Figure 3. VT-^{31}P{^{1}H} NMR of crystals of **1** solubilized in CD_2Cl_2.

Scheme 5. Synthesis Pathway for Fc(P)$_4$^{t}Bu



cies the occurrence of phosphino group migration due to sigmatropic rearrangement (Scheme 6b).[16]

This kind of transposition is probably at the origin of the formation (Scheme 6a) of 1,3-bis(diphenylphosphino)-4-*tert*-butylcyclopentadienes, which upon deprotonation with ^{n}BuLi (step 2 in Scheme 6) would yield 1,3-bis(diphenylphosphino)-4-*tert*-butylcyclopentadienyllithium; the many isomeric forms existing for the corresponding 1,3-bis(phosphino)dienes might favor 1,5-sigmatropic transposition. The formation of 1,1′,2,3′-tetrakis(diphenylphosphino)-4,4′-di-*tert*-butylferrocene would then originate from contamination of 1,2-bis(diphenylphosphino)-4-*tert*-butylcyclopentadienyllithium by 1,3-bis(diphenylphosphino)-4-*tert*-butylcyclopentadienyllithium in the assembly step 3 in Scheme 5. The major change in synthetic procedures relative to the originally published conditions[15a] was clearly the concentration in cyclopentadienyllithium salts. Indeed, concentrations around 1.5×10^{-3} mol·mL^{-1} in toluene were employed, 4-fold higher than the usual conditions reported (about 3.5×10^{-4} mol·mL^{-1}). Deprotonation of quickly formed (diphenylphosphino)cyclopentadienes by some remaining cyclopentadienyllithium salt reactant[7] might help such rearrangements. Further studies are necessary to investigate this side-product formation in cyclopentadienyl—alkali metal salt chemistry; in particular calculations on proton acidity of phosphorylated cyclopentadienes might help in this purpose. Nevertheless the fact that a phosphorylation on a position adjacent to a hindered group on the Cp rings is feasible is a result worth mentioning.

The difficulty encountered in forming tetraphosphine/copper coordination complexes at ambient temperature, whatever the solvent we employed (in priority solvents classically used in catalytic studies), clearly indicates that, as expected, affinity of polyphosphine Fc(P)$_4$^{t}Bu toward palladium is greater (at rt palladium/tetraphosphine complexes immediately form).[6] However, when the temperature is raised to 80 °C, several coordination species with copper salts are observed, and under certain conditions very stable complexes such **1** are even formed. The excess of copper (relative to palladium) usually employed under Sonogashira catalytic conditions statistically augments the opportunity of ligand transfer from palladium to copper. Additionally, the fluxional behavior of CuI toward phosphorus ligation evidenced herein could also be a favorable factor for copper interference in palladium/polyphosphine coordination. Therefore, the opening study reported herein is, from a coordination viewpoint, rather in favor of a possible role of CuI/ligand interaction in the multipart mixture (Pd/Cu/ligand/aryl/alkyne/base/solvent) that characterizes Sonogashira alkynylations. Investigations combining spectroscopic and kinetic methods, like has been done in the evaluation of factors contributing to the accelerating effect of CuI in Stille palladium-catalyzed cross-coupling of aryl iodides with organostannanes,[17] would be of interest on this topic. With the view to directly get valuable insights into the influence of copper/ligand coordination complexes in Sonogashira reactions, a more in-depth study of the catalytic performances obtained under various conditions was then carried out and is described in the following.

Comparative Catalytic Performances of Pd/Cu Tetraphosphine Systems. The three electronically neutral, activated, and deactivated aryl bromides initially employed for coupling with phenylacetylene and the temperature and solvent/base conditions described below were used to reinvestigate the performances obtained in aryl alkynylation with various [(Pd)/(Cu)/(tetraphosphine)] systems. Table 4 summarizes the conditions and results obtained under strict absence of oxygen.[9]

We first checked the origin of phenylacetylene dimerization and enyne formation that hampered the coupling of the more demanding substrate 4-bromoanisole in the preliminary catalytic reactions (Table 1). Experiments conducted with phenylacety-

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(17) Casado, A. L.; Espinet, P. *Organometallics* **2003**, *22*, 1305, and references therein. In this study the authors found that CuI captures part of the free ligand (PPh_3, $AsPh_3$) and consequently moderates their deleterious effect on the rate-determining Sn/Pd transmetalation step.

Scheme 6. Rearrangement in Alkali-Metal Chemistry of Substituted Phosphinocyclopentadienes

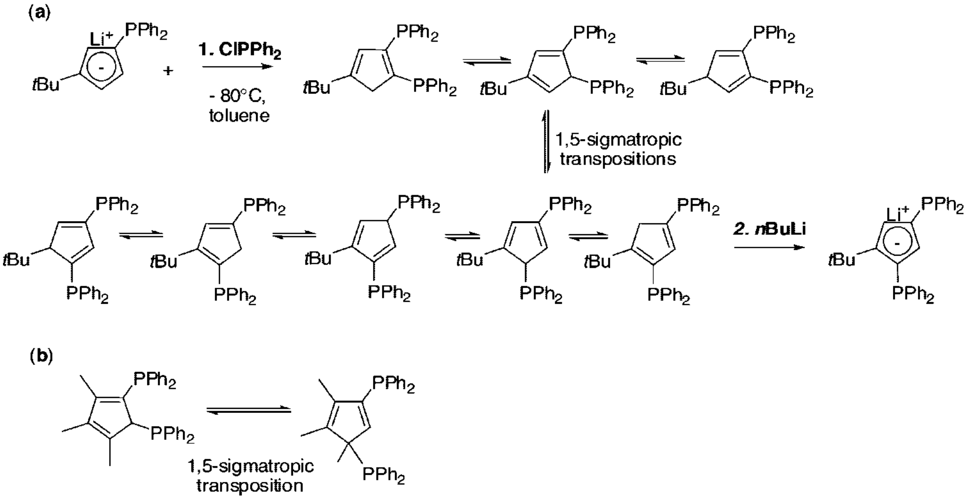

Table 4. Investigation of Aryl Alkynylation with [(Cu)/(Pd)/(Tetraphosphine)] Systems[i]

entry	palladium source	copper source	additional $Fc(P)_4{}^tBu$	aryl bromide	yield in coupling product (%)
1		5 mol % CuI			0[a]
2		5 mol % CuI	1 mol %		0[a]
3		1 mol % complex **1**			0[a]
4		5 mol % CuI		4-bromoanisole	0[a]
5		1 mol % complex **1**		4-bromoanisole	0[a]
6	0.5 mol % $[PdCl(allyl)]_2$	5 mol % CuI		4-bromoanisole	5[b]
7	0.5 mol % $[PdCl(allyl)]_2$		1 mol %	4-bromoacetophenone	100[c]
8	0.5 mol % $[PdCl(allyl)]_2$		1 mol %	4-bromobenzene	89[d]
9	0.5 mol % $[PdCl(allyl)]_2$		1 mol %	4-bromoanisole	22[e]
10	0.5 mol % $[PdCl(allyl)]_2$	1 mol % complex **1**		4-bromoacetophenone	100[f]
11	0.5 mol % $[PdCl(allyl)]_2$	1 mol % complex **1**		4-bromobenzene	98[g]
12	0.5 mol % $[PdCl(allyl)]_2$	1 mol % complex **1**		4-bromoanisole	91[h]

[a] No reactions. [b] 95% unreacted ArBr, phenylacetylene dimerization diyne, and enyne products are obtained.[9] [c] Phenylacetylene dimerization and unidentified heavier products are obtained from phenylacetylene excess. [d] 5% of unreacted ArBr and 5% of heavier benzene products. [e] 70% of unreacted ArBr and 7% of anisole. [f] Traces of diyne from phenylacetylene dimerization. [g] 2% of unreacted ArBr. [h] 9% of unreacted ArBr. [i] Catalytic conditions: (alkyne:aryl) 2:1, 2 equiv of K_2CO_3, 24 h in 10 mL of DMF at 130 °C, GC average yields from two or three runs are given.

lene in the presence of only a copper source (CuI, complex **1**, or mixture of CuI/$Fc(P)_4{}^tBu$) were conducted (entries 1 to 5). In these experiments the starting alkyne and aryl halides were recovered unchanged. It clearly appeared that palladium is absolutely necessary; otherwise no reactions occur with the alkyne in the presence or in the absence of 4-bromoanisole. The pivotal role of palladium in alkyne dimerization was confirmed in the following runs (entry 6), in which the coupling of bromoanisole to phenylacetylene in the presence of CuI and in the absence of tetraphosphine ligand was attempted. Under these conditions only 5% of coupled (aryl)alkyne was obtained, while diyne and enynes are formed in appreciable amounts.

In the next runs (entries 7 to 9) copper-free alkynylation conditions were used, showing that 4-bromoacetophenone and bromobenzene can visibly be coupled to phenylacetylene (100% and 89% yield, respectively) in the absence of copper. More importantly, it was shown that copper has a deleterious effect for bromobenzene coupling when compared to the preliminary results reported in Table 1 (entry 2). Conversely, the coupling of 4-bromoanisole to phenylacetylene was not very successful (22% of coupling product) in the absence of copper (entry 9). Finally, we checked the usefulness of complex **1** as a source of copper (entries 10 to 12). *Much to our surprise* the three electronically neutral, activated and deactivated aryl bromides were very efficiently coupled to phenylacetylene. In particular, the 4-bromoanisole substrate gave 80 to 90% yield of coupling product in the several runs conducted, while under the previous conditions explored this substrate was very reluctant to couple. The apparent reason for this is that the system {$[PdCl(allyl)]_2$/**1**} does not lead to diyne and enyne formation, contrary to the other [Pd/Cu] systems we investigated. To our knowledge, this is the first time that this kind of high selectivity is induced in Sonogashira alkynylation by initial ligand complexation *to copper instead of palladium.* These results demonstrate that coordination of Cu halide cocatalyst in the Sonogashira reaction is a factor that should no longer be neglected. In particular Fairlamb and co-workers have proposed that for terminal alkynes homocoupling Cu(I)/Cu(II) redox systems are necessary to reoxidize Pd(0) to Pd(II).[9] To go further on this idea, it is reasonable to think that the coordination of a ligand on CuI should strongly modify any Cu(I)/Cu(II) redox systems and, therefore, should influence the alkyne dimerization side reactions of the fascinating Sonogashira coupling.

Conclusions

The first examples of copper(I) ferrocenylpolyphosphine complexes were reported. The molecular structures of complexes {*P,P′,P″*-[1,1′,2,2′-tetrakis(diphenylphosphino)-4,4′-di-*tert*-butylferrocene]iodocopper(I) and {*P,P′,P″*-[1,1′,2,3′-tetrakis(diphenylphosphino)-4,4′-di-*tert*-butylferrocene]iodocopper(I)} were solved by X-ray diffraction studies. Copper complexes incorporating phosphine ligands are less common than copper complexes incorporating nitrogen ligands (X-ray structures based on CuP_3 motif are 30 times less numerous than CuN_3 in CSD 06/2007); structures of copper complexes incorporating tetraphosphine ligands are even more rare.[10a] The dynamic behavior of these species in solution was investigated by VT-^{31}P NMR and showed that the CuI fragment has a fluxional behavior over three of the four phosphorus atoms. This type of dynamic activity was interestingly exemplified before with Fc(P)$_4{}^{t}$Bu in palladium coordination chemistry.[6] The synthetic and characterization studies were put in relation with the role of the ligand Fc(P)$_4{}^{t}$Bu in Pd/Cu-cocatalyzed alkynylation reactions to suggest that under the conditions we used interferences of CuI with the ligand cannot be totally excluded.

From the catalytic performances it was clearly shown that 1 mol % of complex **1** is far more efficient and selective for Sonogashira coupling than 5 mol % CuI in the coupling of a set of electronically neutral, activated, and deactivated aryl bromides to phenylacetylene. It avoids the concurrent and deleterious consumption of phenylacetylene by formation of diyne or enynes. Several experiments showed that the use of CuI (or complex **1**) in the absence of a palladium source does not produce any reaction (either aryl alkynylation or phenylacetylene dimerization). Additionally, the use of complex **1** offers practical advantages: it has been used in only 1 mol % against 5 mol % for CuI, and its enhanced stability to air allows a much easier weighing and stocking compared to strictly anhydrous CuI.

Finally, these results suggest that a more systematic examination of the interaction of copper(I) halides with ligands primarily devoted to palladium stabilization in reactions containing the two metals would be of high mechanistic interest. This is especially true for ligands incorporating nitrogen atoms, which are susceptible to transfer to copper,[18] as well as for labile monophosphines such as PPh$_3$,[3a,17] and for alkynylations conducted in acetonitrile solvent,[19] in which robust copper-phosphine complexes might be formed. Finally, enhanced performances could be expected from a ligand chemistry directed to copper in complement to palladium or even from well-defined Pd/Cu bimetallic complexes.

Experimental Section

General Considerations. The reactions were carried out in oven-dried (115 °C) glassware under an argon atmosphere using Schlenk and vacuum-line techniques. Except for methanol and acetonitrile (which were deoxygenated by nitrogen freezing/vacuum) the solvents were distilled over appropriate drying and deoxygenating agents prior to use. ^{1}H (300.13 and 600.13 MHz) and ^{31}P (121.49 and 242.94 MHz) including variable-temperature NMR experiments were performed in CDCl$_3$ or CD$_2$Cl$_2$ on a 600 MHz Bruker Avance II and a 300 MHz Bruker Avance. NMR, UV (Varian Cary 50 spectrophotometer), elemental analyses, and electrospray mass spectrometry (on a Bruker microOTOF-Q instrument) were performed at the Centre de Spectrométrie Moléculaire (CSM) of the Institut de Chimie Moléculaire de l'Université de Bourgogne (ICMUB-UMR CNRS 5260). The UV-visible characterization of the copper complexes was performed in dichloromethane. Continuous wave (CW) EPR experiments were recorded in frozen solution (115 K) on a Bruker ELEXSYS 500 spectrometer equipped with a 4122 SHQE/0405 X-band resonant cavity operating at 9.30 GHz (6 mW power, 100 kHz modulation).

Sonogashira Reactions. The reaction of aryl halide (3.38×10^{-3} mol), phenylacetylene (2 equiv, 0.75 mL), K$_2$CO$_3$ (2 equiv, 0.935 g), and CuI (1.69×10^{-4} mol, 32 mg, or complex **1**, 3.38×10^{-5} mol, 41 mg) at 130 °C during 24 h in DMF (10 mL) in the presence of Fc(P)$_4{}^{t}$Bu (3.38×10^{-5} mol, 35 mg) and [PdCl(η^3-C$_3$H$_5$)]$_2$ (1.69×10^{-5} mol, 6.18 mg), under argon, affords the coupling products. Pure products were obtained after addition of water, extraction with organic solvents, separation, drying, concentration, and chromatography on silica gel.

Tetraphosphine Fc(P)$_4{}^{t}$Bu. The ligand 1,1′,2,2′-tetrakis(diphenylphosphino)-4,4′-di-*tert*-butylferrocene, Fc(P)$_4{}^{t}$Bu, was prepared following the synthesis reported in the literature.[6,15] Chemical shifts of pure product are as follow:[8] ^{1}H NMR (CDCl$_3$): δ 6.40–8.90 (m, 40 H, Ph), 4.14, 4.05 (s, 2 H each, Cp), 0.70 (s, 18H, ^{t}Bu). ^{31}P{^{1}H} (CDCl$_3$): δ −28.6, −32.2 (AA′BB′, $^3J_{AB} = {}^3J_{A'B'} = 74$ Hz, $^{TS}J_{AA'} = 60$ Hz). UV–visible (nm, CH$_2$Cl$_2$): 228, 279 (shoulder), 466. In the ground state, the electronic structure has a strong metal character and is described as being $(3e_{2g})^4(5a_{1g})^2$. The two lower energy absorption bands are assigned to the $5a_{1g} \rightarrow 4e_{1g}$ and $3e_{2g} \rightarrow 4e_{1g}$ transition, respectively; these transitions are metal-centered. The intense LMCT band near 220 nm is assigned to transitions from a π-orbital ligand to the $4e_{1g}$ metal level.

Copper Complexes Synthesis: 1. Anhydrous copper iodide conserved under an argon atmosphere (0.28 g, 1.470 mmol, 4 equiv) and Fc(P)$_4{}^{t}$Bu (0.4 g, 0.387 mmol) were dissolved in degassed acetonitrile (20 mL). The mixture was stirred at 80 °C for 3 h, after which time a pale yellow precipitate was visible. After cooling, the mixture was filtered over Celite and the resulting solution concentrated *in vacuo*. After two days in a freezer at −18 °C, **1** crystallizes as air-stable orange needles in 54% yield (0.25 g, 0.21 mmol), easily separable from cocrystallized square-shaped, white, transparent crystals of the inorganic complex catena-[(μ^3-iodo)(acetonitrile-*N*)copper(I)], arising from excess CuI. C$_{66}$H$_{62}$P$_4$FeCuI (MW 1225.39, exact mass 1224.149): *m/z* 1113.236 (M$^+$ − I + O); 1097.243 (M$^+$ − I), simulated 1097.244 ($\sigma = 0.058$). Anal. Calcd: C 64.69, H 5.10. Found: C 64.62, H 4.97. From single crystals (see spectrum in the Supporting Information), ^{1}H NMR (CDCl$_3$ at 27 °C): δ 6.80–8.10 (m, 40 H, Ph), 4.25, 4.14 (s, 2 H each, Cp), 0.82 (s, 18H, ^{t}Bu), residual uncoordinated acetonitrile gives an intense singlet at 2.02 ppm. ^{31}P{^{1}H} (CDCl$_3$, at 27 °C): δ −23.4 (s), −24.6 (m, br). UV–visible (nm, CH$_2$Cl$_2$): 232, 298 (shoulder), 467. Since copper(I) has fully occupied d-orbitals, no d → d transition occurs for the complexes in the visible region and the UV–visible is similar to the spectrum of the starting ferrocenyl ligand. The electronic spectrum for **1** is only the signature of the ligand; no metal–ligand charge transfer (MLCT) occurs. As evoked for the UV–visible analysis of Cu(I), fully occupied d-orbitals give a diamagnetic EPR-silent complex at 115 K, which is in total agreement with NMR and X-ray diffraction analyses, and shows that no oxidation to Cu(II) occurred. **1b** was eventually obtained concomitantly with **1** from a pool of Fc(P)$_4{}^{t}$Bu contaminated with the unforeseen ligand 1,1′,2,3′-tetrakis(diphenylphosphino)-4,4′-di-*tert*-butylferrocene. 1,1′,2,3′-Tetrakis(diphenylphosphino)-4,4′-di-*tert*-butylferrocene is formed as a byproduct upon modification of the synthetic procedure[15a] to produce Fc(P)$_4{}^{t}$Bu (as explained in Schemes 5 and 6). In particular, a high concentration of ^{t}BuCpLi (1.43×10^{-3} mol·mL^{-1} in toluene) was used in the first step of the synthesis. C$_{66}$H$_{62}$P$_4$FeCuI (MW 1225.39, exact mass 1224.149): *m/z* 1113.246 (M$^+$ − I + O), simulated 1113.239 ($\sigma = 0.388$); 1097.254 (M$^+$ − I). From single crystals (see spectrum in the Supporting Information), ^{1}H NMR (CDCl$_3$ at 27 °C): δ 6.50–8.25 (m, 40H, Ph), 3.95, 4.09, 4.47, 4.58 (s, 1H each, Cp), 0.80 (s, 18H, ^{t}Bu). ^{31}P{^{1}H} (CDCl$_3$, at 27 °C): δ −20.7 (s), −22.9 (m, br), −28.3 (m, br).

X-ray Crystallographic Structure Determination of 1 and 1b. Intensity data were collected on a Nonius Kappa CCD at 115 K. The structures were solved by direct methods (SIR92)[20] and refined with full-matrix least-squares methods based on F^2 (SHELXL-

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97)[21] with the aid of the WINGX program.[22] All non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were included in their calculated positions and refined with a riding model. One phenyl group of the **1b** isomer was found to be disordered over two positions (occupation factors to 0.50:0.50). As for **1b**, one phenyl group of the complex **1** is disordered over two positions (occupation factors: converged to 0.56:0.44). Both components of this disordered phenyl group were refined as rigid groups with anisotropic thermal factors U_{ij} restrained to approximate an isotropic behavior (ISOR). The last Fourier difference maps indicate the presence of a third badly disordered acetonitrile solvate molecule in the asymmetric unit, but any tentative model of this disorder failed. Additionally, the presence of a third solvent molecule is corroborated by the fact that the unit cell volume (3194 Å^3) is very similar to those observed for the isomer **1b** (3205 Å^3), which contains three acetonitrile molecules per asymmetric unit. Crystallographic data are detailed in Table 2.

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Supporting Information Available: Crystal structure data for **1** and **1b** as a CIF file (CCDC 653478 and 653479), NMR spectra corresponding to ref 11, exact mass ES analysis for **1** and **1b**, PovRay illustration of inorganic complex catena[(μ^3-iodo)(acetonitrile-*N*)copper(I)], GC conditions, and analysis from aryl alkynylation reactions. This material is available free of charge via the Internet at http://pub.acs.org.

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