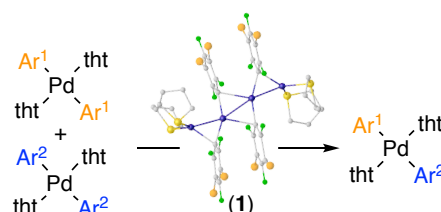


[Cu(C₆Cl₂F₃)(tth)]₄: An Extremely Efficient Catalyst for the Aryl Scrambling Between Palladium Complexes

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ABSTRACT: The copper compound [Cu(C₆Cl₂F₃)(tth)]₄ (**1**) (tth: tetrahydrothiophene) is an excellent catalyst for the *trans*- to *cis*- isomerization of complexes [PdAr₂(tth)₂](Ar: fluoroaryl) and also for the exchange of aryls between those palladium complexes. Herein, we also communicate the synthesis and characterization of **1**, and some of its derivatives. The x-ray structure of **1** shows a linear chain of copper atoms, supported by fluoroaryl rings. The NMR ¹⁹F-DOSY study indicates that this structure is preserved in solution although in equilibrium with other species.



Multimetallic systems are receiving ongoing attention from the organometallic community, due to their role in catalyzed processes.¹⁻³ Unfortunately, the understanding of systems composed by two or more metals is far from complete and the rational design of bimetallic catalytic systems is nowadays an almost unachievable task. Most of the difficulties come from the fact that catalytic cycles are formed by highly reactive organometallic intermediates which can react with complexes containing the second metal as well as with organic substrates, producing unwanted interferences in the reaction pathway. In addition, the exchange of “spectator ligands” or of electrons between the metals may also spoil a “well designed” catalytic cycle.⁴ Considering the difficulties, it is remarkable the large number of multimetallic co-catalyzed processes. Particularly important are bimetallic systems involving copper and palladium. In addition to the Wacker reaction, an historic landmark in catalysis, copper accelerates the Stille cross-coupling, the copper/palladium pair catalyzes many other C-C and C-E coupling reactions including the Sonogashira reaction.¹⁻³ Leaving aside the copper mediated electron-transfer reactions, the role attributed to organocopper in these reactions is to act as transmetalating reagent towards complexes of the type [PdRXL₂] or as ligand scavenger in the “copper effect”,⁵ but there are no reports of the role of copper complexes as catalysts for other reaction steps.³ The hypothetical intervention of organocopper complexes in other steps of the cross-coupling reactions has not been addressed so far.

Here we report new organometallic copper complexes, the study of their ability to catalyze the isomerization reaction of palladium(II) complexes and also the very fast

aryl scrambling that copper(I) produces between aryl palladium complexes.⁵

We have synthesized the complex “CuRf(tth)” (Rf = 3,5-dichloro2,4,6-trifluorophenyl, C₆Cl₂F₃) with the purpose of studying the copper-catalyzed *trans*- to *cis*- isomerization of complexes [PdRf₂(tth)₂], by analogy with related studies with gold complexes.^{6a} In “CuRf(tth)” the Rf group provides extra stability to the C-Cu bond when compared with non-fluorinated aryls,^{7,8} and allows a straightforward ¹⁹F NMR monitoring.⁹ The distinctive feature for organometallic copper(I) compounds is the variability in stoichiometries and the structural diversity of its complexes.^{10,11} Homoleptic compounds “CuR” are usually cyclic oligomers but copper complexes of stoichiometry [CuRL] show typically linear geometry, similar to gold(I) derivatives.¹²⁻²⁰ The only report of linear complexes with tth [CuR(tth)] includes the very encumbered group R = 2,6-bis(2,4,6-triisopropylphenyl)phenyl.²⁰ Trigonal-planar complexes CuRL₂, and oligomers with several other stoichiometries such as [CuRL_{0.5}]_n, are also known.²¹

The synthesis of a complex of formula [CuRf(tth)] was achieved by reacting RfLi with CuBr in the presence of an excess of tth. The ¹⁹F NMR signals of the product are very broad and are not resolved at low temperature, thus an X-Ray structure study was undertaken. The molecular structure is shown in Figure 1 and consists of a chain-copper aggregate of formula [CuRf(tth)]₄ (**1**) where Rf aryls act as the bridges between copper centers, and the four tth ligands are at the ends of the chain. This is a quite unusual structure, the only known linear copper structure similar to that corresponds to the stoichiometry [CuRL_{0.5}]₄, (R:

C_6F_5 ; L: N-heterocyclic germylene NHGes).²² In complex **1** the fluoroaryls seems to form relatively strong three-center two electron bonds, preferring this structure to the use of tht to form four-electron sulfur-bridges.²³ Several complexes of formula $[Cu(C_6F_5)L]$ have been reported, but their structures are linear monomers with the exception of the dimer $[Cu(C_6F_5)(NHGes)]_2$.^{22,24,25}

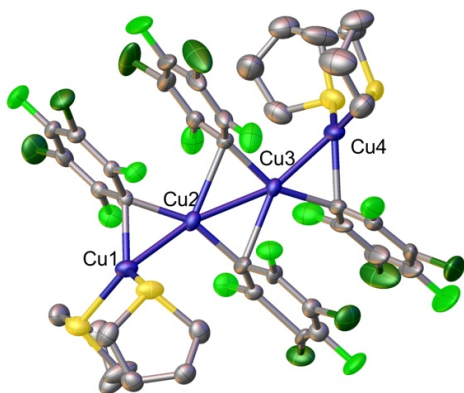


Figure 1. Molecular structure obtained from X-Ray diffraction of complex **1** showing 50% probability ellipsoids. Some selected distances: Cu1-Cu2: 2.4443(9)Å, Cu2-Cu3: 2.5603(8)Å, Cu3-Cu4: 2.4249(9) Å.

As stated above the NMR spectra of **1** are indicative of an equilibrium between complexes. In fact, the addition of tht to solutions of **1** produces a change in the chemical shift and the shape of the ^{19}F NMR, eventually leading to the formation of $[CuRf(tht)_2]$ (**3**) (see scheme in Figure 2). This complex has not been isolated, since the equilibrium is shifted to form **1** during the crystallization, but calculated by DFT calculations predict a planar-trigonal geometry (See SI). The behavior in solution of **1** has been further examined by analyzing the chemical shift and diffusion properties of solutions of **1** with different amounts of tht added. We assumed that the broad NMR signals may contain not only the signals from the inequivalent fluoroaryls in the tetramer **1**, but also signals from homoleptic species $[CuRf]_n$, the trigonal monomer $[CuRf(tht)_2]$ (**3**), and other possible oligomers $[CuRf(tht)]_n$.²⁶ Since the ^{19}F NMR signals are not resolved at -70 °C the complete speciation of the sample is not possible. Nonetheless, the study of the diffusion properties and chemical shift is quite informative.

Figure 2a represents the drift of the chemical shift with the amount of added tht, showing that the chemical shift does not change after the addition of four (or more) tht per $[CuRf(tht)]_4$, thus $[CuRf(tht)_2]$ is the limiting composition and no tetrahedral complexes are formed in relevant concentration. Also, the average diffusion coefficient (D) of the sample has been measured by DOSY experiments at 298 K, leading to the same conclusion (Figure 2b). The diffusion coefficient and the molecular weight are related by the empirical law $D = KM_w^\alpha$ (where K is a constant and α is a coefficient that depends on the size and shape

of the particles).^{27,28} By measuring D for various known fluorinated organometallic complexes, we have found a value of $\alpha = -0.39$ (Figure 2, see also SI).

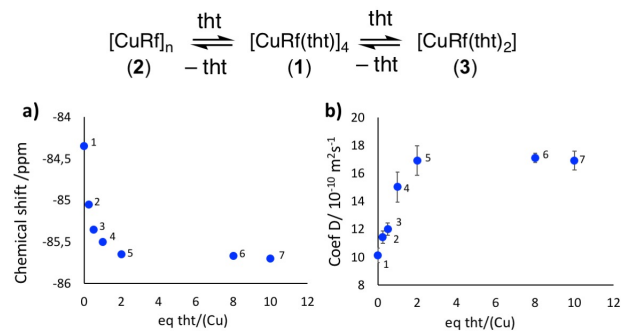


Figure 2. (a) Graphic representation of chemical shift versus equivalents of tht added in THF. (b) Graphic representation of experimental D (D = Diffusion coefficient) obtained from DOSY experiments versus equivalents of tht added THF

The experimental value of $\ln D$ for the mixtures of **1** with different amounts of tht (orange dots in Figure S1) have been interpolated on the line obtaining a “observed molecular weight” (M_{Wobs}) for the samples. The M_{Wobs} value at very high concentrations of tht is 317 ± 125 , that agree with the formation of **3** which has a M_w of 440. The solution without added tht, gives a M_{Wobs} of 1174 ± 184 , being the M_w of **1** 1407. Thus, data suggest that solutions of complex **1** consist of an equilibrium in which the tetramer **1** is the major species, with small amounts of $[CuRf(tht)_2]$ and $[CuRf]_n$ formed by disproportionation. From complex **1** the monomeric complex $[CuRf(4,4'-bipy)]$ (used for diffusion experiments) was easily obtained by substitution of the tht (see x-ray structure and experimental details in SI).

Complexes **1** and **3** (made from complex **1** in the presence of a large excess of tht) have been used to test the copper-catalyzed *trans*- to *cis*- isomerization of palladium complexes $[PdRf_2(tht)_2]$ (complexes **4** and **5**) (eq. 2, Figure 3). The use of these complexes is quite convenient to avoid the exchange of neutral ligands between copper and palladium systems similar to that found in gold(I)/palladium(II) systems.^{4b}

The catalyzed reaction takes place at 25 °C and the observed reaction rate using **1** as catalyst (4% mol) is $k_{obs} = 0.7 s^{-1}Lmol^{-1}$. For $[AuRf(tht)]$ as catalyst at 31 °C k_{obs} is about $5 s^{-1}Lmol^{-1}$.^{6a} Note, however, that since k_{obs} has been calculated assuming that the tetramer **1** is the catalyst, it is plausible that the true catalyst is some fragment of the type “ $CuRf(tht)$ ” present in low concentration in the solution, meaning that the activity of the copper would be much higher. When **3**, prepared by addition of tht to **1**, was used as catalyst a k_{obs} value of $7.10^{-2} s^{-1}Lmol^{-1}$ was obtained (Figure 3b).²⁹ For this concentration of tht, the reaction is much slower and the hydrolysis of the copper complex with the residual water competes with the aryl

exchange, so it has to be considered in the kinetics to obtain meaningful values.

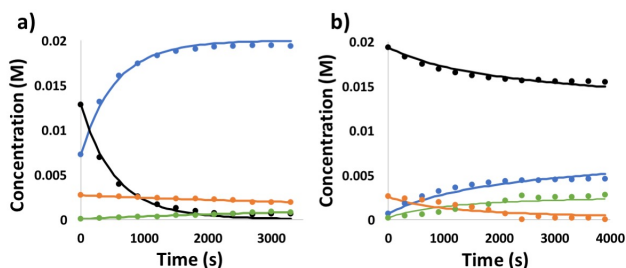
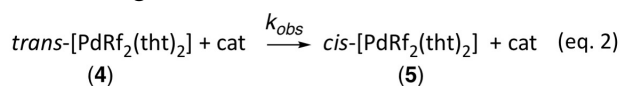
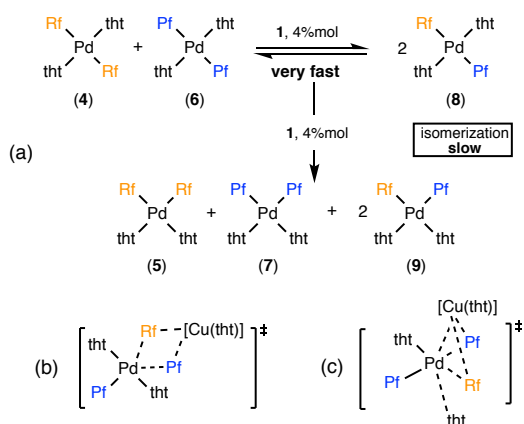


Figure 3. Concentration/time plot of the copper catalyzed isomerization reaction of *trans*-[PdRf₂(tht)₂] (**4**) (black spots) to *cis*-[PdRf₂(tht)₂] (**5**) (blue spots) in THF at 25 °C. Starting concentrations a) [4]₀ = 0.02 M, [CuRf(tht)]₄ 7.5 · 10⁻⁴ M, (no tht added); b) [4]₀ = 0.02 M, [1]₀ = 7.5 · 10⁻⁴ M, and [tht] = 0.063 M.

With the aim of establishing whether the isomerization takes place with or without copper/palladium transmetalation of the aryl group, we tried the isomerization reaction of a mixture of fluoroaryl complexes *trans*-[PdRf₂(tht)₂] (**4**) and *trans*-[PdPf₂(tht)₂] (**6**) (Pf = C₆F₅). In this experiment the formation of the mixed isomer *cis*-[PdRfPf(tht)₂] (**9**) would demonstrate the transmetalation during the isomerization. To our surprise the first spectrum of the series showed the equilibrium of the complexes **4** and **6** with *trans*-[PdRfPf(tht)₂] (**8**) (Scheme 1a). The non-catalyzed aryl exchange between **4** and **6** to produce **8** has been studied and is very slow at 25 °C.³⁰ Thus, the transmetalation is a much faster process than the isomerization, indicating that other steps contribute largely to the rate of isomerization. Once the equilibrium between **4**, **6** and **8** has been established, all of them evolve to the *cis* isomers **5**, **7** and **9** (Scheme 1).



Scheme 1.

In view of these results, the catalyzed aryl exchange between *cis*- complexes **5** and **7** was tested with a similar result: *cis*-[PdRfPf(tht)₂] (**9**) is formed in a very fast

process. The reaction takes place even at -65 °C, with an observed reaction rate at -40 °C of at 3 · 10⁻⁴ s⁻¹Lmol⁻¹ what makes of this an extremely fast reaction for the organo-palladium isomerization or transmetalation standards. The substitution reaction probably involve aryl-copper unsaturated species, capable to form three-center two electron bonds involving also the Pf-Pd bond. Structures 1b and 1c in scheme 1 represent plausible transition states for the aryl-by-aryl and tht-by-aryl substitution reactions respectively that can be involved in the aryl exchange and isomerization reactions. Bimetallic Pd/Cu complexes with electron deficient bonds between these metals and aryl ligands have been synthesized and computationally studied by Chen and coworkers, who have proposed these structures to be models for TS of transmetalation reactions.³¹

In conclusion, fluoroaryl-copper(I) complexes have shown to be very active catalyst for the isomerization and for the scrambling of organic groups between palladium complexes, showing a very small activation energy. Detailed mechanistic studies are ongoing including kinetic and DFT studies.

ASSOCIATED CONTENT

Supporting Information. The supporting information contains: Experimental and computational methods (11 pages). This material is available free of charge via the Internet at <http://pubs.acs.org>

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