Syntheses, Characterizations, and Reactivity of Two Cu(I)-Amido Complexes: Proposed Intermediate in Cu(I)-Catalyzed Goldberg Reaction¹

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Abstract—Reactions between dichloro-bridged copper(I) complexes and amides with different carbonyl substituents (CF₃, CH₃, and Ph) were reported. Two neutral Cu(I)-amido complexes, [Cu(Dppf)(MOAA)] (I) and [Cu(Dppf)(MOTFAA)] (II) (Dppf = 1,1'-bis(diphenylphosphino)ferrocene, MOAA and MOTFAA = deprotonated *N*-(4-methoxyphenyl) acetamide and *N*-(4-methoxyphenyl) trifluoroacetamide, respectively), were synthesized in moderate to good yield and characterized by element analysis, 1H NMR and X-ray crystallography method (CIF file CCDC no. 1015222 (I)). The results showed that the production of Cu(I)amido complxes were influenced by carbonyl substituent in the order of Ph > CF₃ > CH₃. The substituent effect also appeared in the *N*-arylation reactions of I and II with iodobenzene, which generated another copper(I) complex Cu(Dppf)I (III) and two amides products [*N*-methyl-*N*-(4-methoxyphenyl) acetamide] (A) and [*N*-methyl-*N*-(4-methoxyphenyl) trifluoroacetamide] (B) in different yield. The formation and transformation of the Cu(I)-amido complexes could indicate their dynamiccompetency as the intermediates of Goldberg reaction.

Keywords: intermediate, amide, Goldberg reaction, mechanism **DOI:** 10.1134/S1070328418050044

INTRODUCTION

At the beginning of twenty century, Irma Goldberg reported his pioneering work on copper-mediated Goldberg reaction [1]. From then on, the arylation of amide has received considerable attentions [2]. However, original coupling reactions suffered from stoichiometric amounts of copper salts, high reaction temperature and long reaction time [3]. Recently, many drawbacks of the classical reaction have been overcome by adding organic ligand to the copper catalyst [4, 5]. At present, Goldberg reaction has become an efficient method to form C–N bonds in organic synthesis, pharmaceuticals and polymer science [6].

Besides developing new ancillary ligands, the mechanism study can help to improve the reaction conditions and broaden the reaction scope. Isolation and detection of intermediate is one of the most used methods to unravel reaction mechanism. However, only few intermediates were isolated in pure form due to their light or air-sensitivity, making their isolation Herein, the reactions of dichloro-bridged copper(I) precursor with amides bearing electron-, electron-donating and hindered carbonyl substituent (CF₃, CH₃, Ph) have been studied. Considering the extreme air-sensitivity of reaction intermediate, 1,1'bis(diphenylphosphino)ferrocene (Dppf) with strong chelating ability and reducibility was used as main ligand to prepare precursor. Two Cu(I)-amido complexes [Cu(Dppf)(MOAA)] (I) and [Cu(Dppf)-(MOTFAA)] (II) MOAA and MOTFAA is deprotonated *N*-(4-methoxyphenyl) acetamide and *N*-(4methoxyphenyl) trifluoroacetamide, respectively) were prepared and characterized by IR, element analysis and ¹H NMR. Their *N*-arylation reactions with aryl halide were also reported.

and characterization difficult [7-10]. However, the effect of substituent groups of amide on the synthesis of intermediate was not reported. In theory, the substituent group, especially the carbonyl substituent near the reactive site (NH substrate), could influence the Lewis acidity of amide, and as well as the synthesis of reaction intermediates.

¹ The article is published in the original.

EXPERIMENTAL

Materials and methods. Dppf, trifluoroacetic acid, 4-methoxy aniline and other chemicals were obtained from commercial sources. All solvents were dried by common methods and freshly distilled prior to use. Dichloro-bridged copper(I) complex [(Dppf)Cu]₂(μ -Cl)₂] and substituted amides were synthesized according to literatures [11, 12]. Synthetic procedures were carried out under a nitrogen atmosphere using a standard Schlenk flask considering the air and moisturesensitivity of Cu(I) species. ¹H NMR (400 MHz) was collected on a Bruker ACF-400 spectrometer. Elemental analyses for C, H, and N were carried out on a Bio-Rad elemental analyzer. Thermogravimetric (TG) analysis was carried out using an Exstar 6000 analyzer in nitrogen at a heating rate of 15°C min⁻¹. Electron spray ion (ESI) mass spectrum was measured using a Waters Platform ZMD4000 LC/MS mass spectrometer.

The synthesis route of the Cu(I)-amido complexes are shown in Scheme 1:



 $R = CF_3(I), CH_3(II), Phenyl (----)$

Scheme 1.

Synthesis of complex I. Dichloro-bridged precursor $[(Dppf)Cu]_2(\mu$ -Cl)_2] (0.131 g, 0.1 mmol), 2,2,2-trifluoro-*N*-(4-methoxy-phenyl)-acetamide (0.055 g, 0.25 mmol) and CH₃ONa (0.054 g, 1.0 mmol) were placed in a Schlenk tube and CH₂Cl₂ (20 mL) was added via syringe under nitrogen atmosphere. The mixture was stirred at room temperature for 48 h. The solvent was removed by rotary evaporator. Yellow block crystals of complex I were obtained by re-crystallization in diethyl ether. The yield was 0.131 g (80%).

IR (v, cm⁻¹): 1634 v(C=O), 1481 vPh(C=C), 1435 vCp(C=C), 1236 v(C-F), 1165 δ Ph(CH), 1099 v(P-Ph), 1032 δ Cp(CH), 823 π Cp(CH). ¹H NMR (400 MHz; CD₂Cl₂; δ , ppm): 7.45–7.37 (m., 12H, Ph), 7.33 (t., *J* = 7.3 Hz, 8H, Ph), 6.96 (d., *J* = 8.7 Hz, 2H, Ph of amide), 6.67 (d., *J* = 8.7 Hz, 2H, Ph of amide), 4.37 (s., 4H, Cp), 4.12 (s., 4H, Cp), 3.76 (s., 3H, OMe).

For $C_{43}H_{35}NO_{2}F_{3}P_{2}FeC$	H35NO2F3P2Fe	Cu
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Anal. calcd., %	C, 61.77	H, 4.22	N, 1.68
Found, %	C, 61.98	Н, 4.52	N, 1.73

Synthesis of complex II. The synthesis was identical to that of complex I, except that 2,2,2-trifluoro-*N*-*p*-tolyl-acetamide (0.051 g, 0.025 mmol) was used as auxiliary ligand. Complex II was prepared as orange crystals. The yield was 112 g (68%).

IR (v, cm⁻¹): 1614 v(C=O), 1497 vPh(C=C), 1432 vCp(C=C), 1262 v(C-F), 1164 δ Ph(CH), 1095 v(P-Ph), 1024 δ Cp(CH), 837 π Cp(CH). ¹H NMR (400 MHz; CDCl₃; δ , ppm): 7.49–7.41 (m., 12H, Ph), 7.36 (t., *J* = 7.4 Hz, 8H, Ph), 7.07 (d., *J* = 8.2 Hz, 2H, Ph of amide), 6.98 (d., *J* = 8.0 Hz, 2H, Ph of amide), 4.40 (s., 4H, Cp), 4.18 (s., 4H Cp), 3.78 (s., 3H, OMe), 2.35 (s., 3H).

For C₄₄H₃₇NO₂F₃P₂FeCu

Anal. calcd., %	C, 62.17	H, 4.39	N, 1.65
Found, %	C, 63.08	Н, 4.32	N, 1.76

X-ray crystallography. A suitable yellow single crystal of complex I with dimensions of $0.48 \times 0.36 \times 0.22$ mm was selected for measurement. Diffraction data for I was collected at 296(2) K using a Bruker SMART APEX II CCD area detector diffractometer (Mo K_{α} , $\lambda = 0.71073$ Å). A total of 30239 reflections

 Table 1. Crystallographic data and refinement parameters of complex I

Table 2. Selected bond distances (Å) and bond angles (deg) for complex \boldsymbol{I}

or complex 1		for complex I		
Parameter	Value	Bond	d, Å	
Fw	836.05	Cu–N	1.975(4)	
Color; crystal form	Yellow; block	Cu–P(1)	2.237(1)	
Crystal system	Monoclinic	Cu–P(2)	2.265(1)	
Space group	$P2_{1}/n$	C(37)–N	1.437(6)	
a, Å	9.7292(7)	N-C(36)	1.315(6)	
b, Å	22.4542(15)	Angle	ω, deg	
<i>c</i> , Å	17.2056(12)	NCuP(2)	128 6(1)	
β, deg	90.591(4)	NCuP(1)	117.6(1)	
<i>V</i> , Å ³	3758.6(5)		117.6(1)	
Ζ	4	P(2)CuP(1)	112.4(5)	
$\rho_{calcd}, g\ cm^{-3}$	1.477	were collected in the range of $2.39^{\circ} \le \theta \le 27.55^{\circ}$ by using the ω -2 θ scan mode, of which 8754 were unique with $R_{int} = 0.0497$. The crystal structure was solved by Direct Methods and refined by full-matrix least squares on F^2 using the SHELXL-97 software [13, 14] All non-hydrogen atoms were refined anisotropically Hydrogen atoms were generated geometrically and treated by a mixture of independent and constrained refinement. The crystallographic data as well as details of data collection and refinements are summarized in Table 1. Selected bond distances and bond angles are shown in Table 2. Supplementary material for structure I has been deposited with the Cambridge Crystallographic Data Centre (CCDC no. 1015222; www.ccdc.cam.ac.uk/ data_request/cif).		
μ , mm ⁻¹	1.090			
<i>F</i> (000)	1712			
Crystal size, mm	$0.48 \times 0.36 \times 0.22$			
θ Range, deg	2.39-27.55			
Index range	$-12 \le h \le 12,$ $-29 \le k \le 25,$ $-21 \le l \le 22$			
Reflections collected/unique (R_{int})	30239/8754 (0.0497)			
Reflections with $I > 2\sigma(I)$	6162	<i>N</i> -Arylation reaction of iodobenzene are shown in flock containing complex.	f complexes I and II with a Scheme 2. To a Schlenk or $\mathbf{H}(0 \mid \text{mmal})$ indepen	
Number of refinement parameters	479	zene (0.020 g, 0.1 mmol) v solvent under nitrogen atm	was added 25 mL DMF as osphere. The reaction mix-	
$R_1, wR_2 (I \ge 2\sigma(I))$	0.0741, 0.1246	ture was stirred at 110°C o tem was concentrated to ab	vernight. The reaction sys- bout 2 mL and left to stand	
Goodness of fit on F^2	0.981	overnight at room temperature. Then a yellow powder (III) was obtained by filtration. The <i>N</i> -arylation prod- uct (A or B) was separated from the filtrate by TLC using ethyl acetate—petroleumether (1 : 10) as devel- oping solvent.		
Largest diff. peak and hole, $e Å^3$	0.749/-0.487			





A: R = CF₃, 65% B: R = CH₃, 52%

Scheme 2.

III: yellow microcrystal, ESI MS (+): 617 [Cu(Dppf)]⁺.

A: yellow powder, 0.019 g, 65%. IR (v, cm⁻¹): 1705, 1507, 1396, 1228, 1203, 1153, 1137, 1016, 957, 820, 767, 748, 717. ¹H NMR (400 MHz; DMSO; δ , ppm): 7.18 (d., J = 8.8, 8.3 Hz, 6H), 7.05 (d., J = 9.0 Hz, 3H), 3.32 (s., 3H).

B: white powder, 0.013 g, 52% yield. IR (v, cm⁻¹): 1672, 1509, 1371, 1298, 1247, 1033, 832, 696. ¹H NMR (400 MHz; DMSO; δ, ppm): 7.43–7.36 (d., J =



Fig. 1. Coordination environment of the Cu(I) centre in complex I. Hydrogen atoms are omitted for clarity.

6.4 Hz, 4H), 7.31–7.27 (d., J = 5.4 Hz, 1H), 7.16–7.13 (d., J = 6.7 Hz, 4H), 3.76 (s., 3H), 2.03 (s., 3H).

RESULTS AND DISCUSSION

Dichloro-bridged copper(I) complex is designed as reaction precursor to improve the solubility and stability of Cu(I) catalyst. To get adequate amide anion, ten-equivalent CH₃ONa is added to the reaction system. Considering the weak acidity of methanol ($pK_a =$ 29.0 in DMSO), strong base CH₃ONa can easily remove the proton of all amide ligands. However, no product was prepared when amide with bulky carbonyl substituent (Ph) reacted with precursor, which shows that steric substituent has a major effect on the formation of intermediate. The result looks like but is not contradictory to the "One-pot" formation of N-aryl benzamide because during which the intermediate can soon convert into the N-aryaltion product and even trace intermediate can be effective [15]. Electronic substituent has a secondary effect on the coordination reaction. In detail, electron with drawing CF₃ group increases the acidity of amide, and thus, the amide anion is easily formed and high yield of intermediate I (80%) is prepared. Instead, electron-donating CH₃ group makes the corresponding amide have weak cidity and intermediate II is prepared at moderate yield (68%).

X-ray diffraction analysis of complex I is carried out and the crystal structure is shown in Fig. 1. Unfortunately, crystal II is easily efflorescent in air in less than one minute, so its crystal structure is difficult to be determined by X-ray diffraction method. Figure 1 shows that the Cu(I) centre is three-coordinated by





Fig. 2. Views of the crystal packing linked by π ... π and C–H...O interactions in complex I: 2D layer (a) and 3D supramolecular framework (b).

one nitrogen atom (Cu–N (1.975(4) Å) from the amide anion and chelated by two phosphine atoms (Cu–P(1) 2.265(1), Cu–P(2) 2.237(1) Å) from the Dppf ligand. The sum of all angles around the Cu(I) centre is $358.6(7)^{\circ}$ and the Cu⁺ ion is 0.147(3) Å above the plane P(1)–P(2)–N, which verifies the slight deviation from ideal trigonal planar environment.

Complex I is assembled into a dimer via interdigitation of aromatic rings with a face-to-face $\pi \cdots \pi$ interactions (brown bond in Fig. 2a) with 3.662(5) Å for perpendicular distance and 3.826(2) Å for centroid distance. The dimers are linked by four C–H···O interactionsinto a two-dimensional layer parallel to the crystallographic *yz* plane (Fig. 2a). Adjacent layers are further connected by one weak C–H···O (orange dotted line) and four C–H···F interactions (blue dotted lines, Fig. 2b) into a three-dimensional suparmolecular framework. Four relative strong C–H···F interactions also play an important role in constructing the crystal construction of I [16, 17]. These partly explain why the crystal structure of I is more stable than II.

To determine the thermal competence of the intermediates, TG analyses of complexes I and II were recorded (Fig. 3). Herein we selected I as a represen-



Fig. 3. TG curves of complexes I and II.

tative to discuss the thermal behaviour. The result shows that I is stable from 50 to 245° C. There are two obvious and continuous stages (~238–380°C) in the process of thermal decomposition, corresponding to the gradual decomposition of organic ligands. The final residues are considered to be copperoxide and ferric oxide, who account for 22.10% (calcd. 22.84%). The TG experiments indicate complexes I and II are thermally stable and qualified as reaction intermediates of Goldberg reaction.

Stoichometric reactions of complexes I and II with iodobenzene are performed under optimized conditions (Scheme 2). Another Cu(I) complex (Dppf)CuI (Scheme 2, III) has been isolated via concentration and settling process and identified by LC-MS-MS analysis. The N-arylated amides A and B are obtained in moderate yields (65 and 52%, respectively) and confirmed by ¹H NMR. Compared with CH₃, electron-withdrawing CF₃ makes the intermediate react with iodobenzene at a relatively higher yield. Considering the well-known oxidative addition reaction (the rate-limiting step of aryl halides activation), weak coordination of fluorine atom outweighing electronic effect increases the electron density of Cu(I) centre. As a result, complex I react with iodobenzene in a higher conversion than complex II.

Thus, the catalytic cycle of Goldberg reaction is simulated including the synthesis and *N*-arylation reaction of intermediates. The intermediate features Cu(I) surrounded by one N atom of amide anion and two P atoms from Dppf. The formation of intermediate is mainly affected by steric effect of amide and is also affected by electronic effect in the order of $CF_3 >$ CH_3 . The *N*-arylation reaction of intermediate with iodobenzene is more affected by weak coordination effect compared with electronic effect of the intermediate.

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