

Pd/Cu-Catalyzed Dehydrogenative Coupling of Dimethyl Phthalate: Synchrotron Radiation Sheds Light on the Cu Cycle Mechanism

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ABSTRACT: Pd/Cu-catalyzed dehydrogenative coupling of dimethyl phthalate is an important industrial process for the production of aromatic polyimide precursors. Nonetheless, the detailed mechanism of the Cu cycle has remained unclear. The present study describes the detailed mechanism of the Cu cycle in the $[Pd(OAc)_2]/Cu(OAc)_2/1,10$ -phenanthroline (phen) system. The solution-phase X-ray absorption fine structure analysis of the catalyst solutions and the FEFF fitting as well as the evaluation of the catalytic and stoichiometric reactions reveal the following observations: (i) the major intermediate in the catalytic cycle is a mononuclear divalent $[Cu(OAc)_2] \cdot 2H_2O$ species, (ii) coordination of the phen ligand to the Cu catalyst significantly inhibits the catalytic activity, (iii) 2 equiv of $Cu(OAc)_2 \cdot H_2O$ oxidizes the zerovalent "Pd(phen)" species to divalent $[Pd(OAc)_2(phen)]$, and



(iv) the divalent $[Cu(OAc)_2]_2$ ·2AcOH species is regenerated by the treatment of monovalent Cu(OAc) with AcOH in air. KEYWORDS: dehydrogenative coupling, dimethyl phthalate, mechanism, Cu catalysis, XAFS

INTRODUCTION

Pd/Cu-catalyzed dehydrogenative coupling of dimethyl phthalate is an industrially important process for the production of aromatic polyimide precursors. It typically involves a catalytic system consisting of $[Pd(OAc)_2]$ (1a), $Cu(OAc)_2 \cdot H_2O$ (2a·H₂O), and 1,10-phenanthroline·H₂O (phen·H₂O) in the absence of any solvent (eq 1).^{1,2} Despite its industrial significance, the detailed mechanism of this process has largely remained unknown. We recently reported the mechanism of this reaction evaluated by solution-phase Xray absorption fine structure (XAFS) using Pd K-edge.³ We also described an alternative synthesis of the intermediates as well as their catalytic and stoichiometric reactions. In this study, Pd complex 1a was easily converted in situ to $[Pd(OAc)_2(phen)]$ (1b), which reacted with dimethyl phthalate (3) to give $[Pd(OAc)\{C_6H_3(CO_2Me)_2-3,4\}(phen)]$ (1c). Subsequently, disproportionation of 1c giving [Pd- $\{C_6H_3(CO_2Me)_2-3,4\}_2(phen)\}$ (1d) and 1b and reductive elimination between the dimethyl phthalyl groups in 1d yielded tetramethyl 3,3',4,4'-biphenyltetracarboxylate (4) with regeneration of 1b (Scheme 1). This study established the mechanism of the Pd cycle; however, the corresponding Cu cycle remained unexplored.



To the best of our knowledge, no systematic study on the Cu cycle in this process has been reported to date. Nevertheless, it is widely accepted that the role of the Cu complex is similar to the Wacker process.⁴ In other words, 2 equiv of the Cu(II) species oxidizes the Pd(0) species 1e *in situ*, and the resulting Cu(I) is oxidized in the presence of acetic acid (AcOH) under oxygen (Scheme 1). In some cases of related catalytic processes involving 1a and 2a, the formation of a heterodinuclear Pd-Cu complex has been

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Scheme 1. Proposed Catalytic Cycle for the Dehydrogenative Coupling of Dimethyl Phthalate Catalyzed by [Pd(OAc)₂]/Cu(OAc)₂/phen



proposed; however, the reaction mechanism of the Cu catalyst still remained mostly unknown.^{5,6} Consequently, we focused on utilizing the XAFS method to elucidate the mechanism of the Cu catalyst in this dehydrogenative coupling. Pioneering applications of XAFS to study the homogeneous Cu catalyst systems were reported for the arylation of acetylacetone⁷ using various Cu(I), Cu(II), and Cu(III) complexes,^{7b} as well as for the Wacker-type oxidation of 1-octene.^{7c} In the present paper, we report the first detailed mechanism of the Cu cycle in the Pd/Cu-catalyzed dehydrogenative coupling. The mechanism was evaluated by solution-phase XAFS experiments using Cu K-edge and by conducting catalytic and stoichiometric reactions. This study suggests the in situ-formed mononuclear divalent complex, $[Cu(OAc)_2] \cdot 2H_2O$ (6a $\cdot 2H_2O$), to be responsible for the catalytically active species to oxidize the Pd(0) species.

RESULTS AND DISCUSSION

Solution-Phase XAFS Analysis of $Cu(OAc)_2 \cdot H_2O$ (2a-H₂O) and Cu(OAc) (2c). To understand the catalytic behavior of the Cu complex in the Pd/Cu-catalyzed dehydrogenative coupling of dimethyl phthalate (3), we conducted a solutionphase XAFS study in 3. Synchrotron radiation was utilized on the SPring-8 BL01B1 beamline using a Cu K-edge (8.978 keV) in the fluorescence mode. All solutions were filtered through a polytetrafluoroethylene (PTFE) membrane filter (0.2 μ m), and the measurements were performed at room temperature.⁸

Cu(OAc)₂·H₂O (2a·H₂O) and Cu(OAc) (2c) species were sparingly soluble in 3. Heating to 120 °C was necessary to dissolve the compounds in 3 in air. On the other hand, [Cu(OAc)₂(phen)]·0.5H₂O (2b·0.5H₂O) exhibited higher solubility in 3 at room temperature and it completely dissolved at 120 °C. Figure 1 illustrates the solution-phase X-ray absorption near edge structure (XANES) spectra of these Cu complexes in a solution of 3. The spectra of solid Cu₂O (black dotted line) and CuO (orange dotted line) are also shown for references of Cu(I) and Cu(II), respectively. Generally, Cu(I) complexes display a strong pre-edge assigned to the 1s \rightarrow 4p electronic transition, with rising edge shoulders occurring in



Figure 1. Normalized Cu K-edge solution phase XANES spectra of $2a \cdot H_2O$ (red), $2b \cdot 0.5H_2O$ (blue), and 2c (green) in 3, as well as solid state Cu₂O (black dotted line) and CuO (orange dotted line). The red and green lines are nearly identical.

the range of 8.983–8.985 keV.⁹ Moreover, the Cu(II) complex exhibits a very weak absorption at 8.979 keV, which corresponds to the forbidden 1s \rightarrow 3d transition. It is also noteworthy that many Cu(II) complexes display intense absorption in the range 8.986–8.988 keV (1s \rightarrow 4p).⁹ The XANES spectra of both 2a·H₂O (red) and 2c (green) in 3 entirely overlap, with the highest peak noted at 8.997 keV. The shoulder peaks (1s \rightarrow 4p_{π}) for 2a·H₂O and 2c are also analogous. These observations confirm the formation of 2a-H₂O from 2c. Namely, the valence of the Cu(I) complex changes to Cu(II) upon dissolution in 3 at 120 °C. Furthermore, disproportionation of 2c is the likely process leading to this transformation.¹⁰ In fact, Lei and co-workers have previously proposed a similar disproportionation reaction of a Cu(I) complex to Cu(II) and Cu(0) species.^{7a}

The extended X-ray absorption fine structure (EXAFS) spectra of the three Cu complexes in 3 are illustrated in Figure 2. The spectra of $2a \cdot H_2O$ (red) and 2c (green) dissolved in 3 are nearly identical, as expected based on their XANES spectra. Moreover, the EXAFS spectra are analogous to the previously reported EXAFS of crystalline $2\mathbf{a} \cdot \mathbf{H}_2 \mathbf{O}_2^{11}$ suggesting the formation of $2a \cdot H_2O$ from 2c. The *r*-space graphs are obtained by the Fourier transform of the k-space data and exhibit characteristic peaks, which correspond to Cu-O (1.56 and 2.08 Å in radial distance¹²) and Cu-Cu (2.49 Å in radial distance), implying the existence of a dinuclear species of 2a. H₂O. Importantly, according to the molecular structures obtained by single-crystal X-ray diffraction (XRD), 2a·H₂O adopts a paddle wheel-shaped dinuclear structure [Cu(μ -OAc)₂]₂·2H₂O (Cu-OAc: 1.969 Å, Cu-OH₂: 2.156 Å, and Cu-Cu: 2.616 Å) (Chart 1).¹³ In addition, the single-crystal XRD of monovalent copper 2c indicates the formation of a bridged 8-membered ring (Cu-OAc: 1.889-1.903 Å, external Cu-OAc: 2.304-2.314 Å, and Cu-Cu: 2.557 Å).¹⁴ Overall, the XANES spectra support the conversion of Cu(I) to Cu(II) in 3, and the suggested Cu(II) species is consistent with the structure of 2a.

In the crystal structure, complex **2b** exists as a water-bridged dimer of the square-planar complex $[Cu(OAc-\kappa^1O)_2(phen)]$;¹⁵ however, in solution, it is suspected to be present as a mononuclear complex.¹⁶ X-ray structure analysis also allowed for the determination of the bond lengths in the complex, including Cu–OAc (1.941–1.959 Å), Cu–OH₂ (2.289 Å), Cu–N (2.023 Å), and Cu–Cu (4.29 Å). Although **2b** contains



Figure 2. Cu K-edge solution phase EXAFS spectra of $2a \cdot H_2O$ (red), $2b \cdot 0.5H_2O$ (blue), and 2c (green) in 3 without phase shift. The *r*-space graph obtained by the Fourier transform in the same *k*-range $(3-11 \text{ Å}^{-1})$ of the top graph, *i.e.*, the *r*-space graph, is illustrated at the bottom.

Chart 1. Molecular Structures of $Cu(OAc)_2 \cdot H_2O$ (2a $\cdot H_2O$), [$Cu(OAc)_2(phen)$] $\cdot 0.5H_2O$ (2b $\cdot 0.5H_2O$), and $Cu(\mu \cdot OAc)$ (2c).



Cu–N and Cu–O bonds, it is difficult to distinguish them by EXAFS because of the resolution of the interatomic distance (~0.1 Å). A significant difference between **2b** (blue) and **2a** (red) in the *r*-space graph is found at approximately 2.5 Å in the radial distance (Figure 2), as there is no direct interaction

Table 1. Controlled Catalysis of XAFS Experiments^b

between the Cu centers in 2b, while 2a has a dinuclear structure.

Solution-Phase XAFS Analysis of Controlled Catalysis. The $[Pd(OAc)_2(phen)]$ (1b)/Cu-catalyzed dehydrogenative coupling of 3 was performed at 200 °C for 1 h under O₂ (0.1 MPa), and the XAFS spectrum of the catalytic solution was measured using Cu K-edge. Although the standard catalytic conditions are as follows: [1b]: 4.00 mM (0.0653 mol %), [2a]: 1.20 mM (0.0196 mol %) in 3 (25 mL), at 200 °C for 6 h in air, the reactions for the XAFS experiments were carried out at higher catalyst concentrations: [1b]: 25 mM (0.408 mol %), [2a]: 7.5 mM (0.123 mol %) in 3 (25 mL) at 200 °C for 1 h to gain a better S/N ratio. Under these conditions, the biaryl products were obtained in 7.4% yield (Table 1, entry 1). Furthermore, the turnover number (TON) based on the Cu catalyst reached 15 (TON = 9 for Pd), which was determined by gas-liquid chromatography (GLC) analysis.

Dehydrogenative coupling of 3 catalyzed by $1b/2b \cdot 0.5H_2O$ and 1b/2c was also performed under the same conditions and resulted in the formation of biaryl products in 2.8% yield and with a TON of 6 (TON = 3 for Pd), and in 8.3% yield and with a TON of 17 (TON = 10 for Pd), respectively (Table 1, entries 2 and 3). Thus, on average, in all cases, several catalytic cycles have been accomplished that the initial Cu complex would have been cycled into some sort of intermediate, and the phen complex of Cu(II) $2b \cdot 0.5H_2O$ showed a lower catalytic activity.

Notably, the XANES spectrum of the catalytic solutions following the catalysis using 2c (yellow) is completely overlaid with 2a (black), as shown in Figure 3, and the top peak reaches



Figure 3. Cu K-edge solution phase XANES spectra of $1b/2a \cdot H_2O$ (black) and 1b/2c (yellow) after catalysis.

8.996 keV. This suggests that the valency of the Cu complex in the intermediate is +2 because these XANES spectra show the

	/ 1					
		3	dimers		TC	DN
entry	Cu catalyst	conv./% ^a	yield/% ^b	4/5	Pd	Cu
1	$Cu(OAc)_2 \cdot H_2O$ (2a·H ₂ O)	20.4	7.4	90/10	9	15
2	$[Cu(OAc)_2(phen)] \cdot 0.5H_2O (2b \cdot 0.5H_2O)$	21.6	2.8	88/12	3	6
3	Cu(OAc) (2c)	22.8	8.3	91/9	10	17

^{*a*}Pd-catalyzed dehydrogenative coupling of dimethyl phthalate (**3**) using Cu(OAc)·H₂O (**2a**·H₂O), [Cu(OAc)₂(phen)]·0.5H₂O (**2b**·0.5H₂O), or Cu(OAc) (**2c**) for the Pd-catalyzed dehydrogenative coupling of dimethyl phthalate. ^{*b*}Conditions: [**1a**] = 25 mM (0.408 mol %), [Cu catalyst] = 7.5 mM (0.123 mol %), **3**: 25.0 mL, O₂ bubbling (0.1 MPa), 200 °C, 1 h. Conversion, yield of dimers, and TON were determined by GLC after the XAFS experiment.

characteristics of Cu(II) species as discussed above. Moreover, the EXAFS *r*-space graph implies that the primary coordination spheres of the Cu species starting from 2a or 2c are equivalent, and the Cu–O bond remains intact; however, the peak resulting from the Cu–Cu interaction is significantly diminished. This indicates that the dinuclear structure nearly collapses during catalysis (Figure 4).



Figure 4. Cu K-edge solution phase EXAFS spectra of $1b/2a \cdot H_2O$ (black) and 1b/2c (yellow) following catalysis and of $2a \cdot H_2O$ (red) in 3 without phase shift. The peak heights of the three curves in the *r*-space graph, that are obtained by the Fourier transformations with the same *k*-range $(3-11 \text{ Å}^{-1})$, are normalized at their primary coordination sphere.

Figure 5 illustrates the EXAFS spectra before (yellow) and after (green) the catalysis initiated by the $1b/2b\cdot 0.5H_2O$ system. For reference, the EXAFS spectrum of $1b/2a\cdot H_2O$ after catalysis (black) is also shown. The EXAFS *k*- and *r*-space graphs show a good coidentity between the green and black curves. One explanation for this observation is the removal of the phen ligand from the Cu center during the catalysis. In fact, we have previously reported the presence of an induction period in the time-course curves of 2b; however, no induction period was observed when 2a was used as the Cu catalyst.³ The inhibitory effect of the phen ligand on the Cu catalyst in the dehydrogenative coupling is discussed in more detail below.

In these experiments, the catalytic reaction was conducted at 200 $^{\circ}$ C, but the XAFS spectrum was observed at room temperature. Therefore, there may be controversy as to whether the observed species really sees the active species in the catalytic cycle. This question is always raised in XAFS



Figure 5. Cu K-edge solution phase EXAFS spectra of the 1b/2b· 0.5H₂O system before (yellow) and after (green) catalysis without phase shift. A catalytic system of 1b/2a·H₂O after the catalysis (black) is also shown. The peak heights in the *r*-space graph are normalized at their primary coordination sphere.

studies, but it cannot be denied that the observed species is in a resting state.

FEFF Analysis of EXAFS. To elucidate the intermediate or resting state in the catalytic solution, we performed the FEFF analysis of the obtained EXAFS spectra. In the present study, the FEFF6 program embedded in Artemis software¹⁷⁻¹⁹ was used to be in agreement with a previous study on the Pd cycle.³ As described above, the divalent Cu(OAc)₂·H₂O (2**a**·H₂O) species actually forms a dinuclear paddle wheel structure, such as $[Cu(OAc)_2]_2\cdot 2H_2O$ (Chart 1). In the current section, we distinguish between the mononuclear $[Cu(OAc)_2]$ (2**a**) complexes.

To the best of our knowledge, the mononuclear complex $[Cu(OAc)_2]$ (6a) has never been isolated from the dinuclear form $[Cu(OAc)_2]_2$. However, the molecular structure of the mononuclear complex $[Cu(OAc)_2] \cdot 2H_2O$ (6a $\cdot 2H_2O$) obtained by single-crystal XRD, along with a brief description of its preparation from $Cu(CO_3)_2(OH)_2$, was previously reported.²⁰ This complex exhibits a very distorted octahedral structure having an intermediate contribution between $OAc - \kappa^2 O_i O'$ and $OAc - \kappa^1 O_i$. Because the complex is the only example of mononuclear copper acetate, we employed the X-ray data for 6a·2H₂O for the initial atomic coordinates in the FEFF analysis. Moreover, we utilized the single-crystal XRD data on the paddle wheel complex $[Cu(\mu - OAc)_2]_2 \cdot 2AcOH$ (2a·AcOH) (vide infra) as the dinuclear species for the FEFF analysis. The r-space graph-based metrical parameters of the FEFF fitting determined by the crystallographic data for 6a- $2H_2O$, the optimized structure of $6a \cdot 2H_2O$ obtained by density functional theory (DFT) calculations at the UB3LYP/6-31G(d,p) level using a polarized continuum model (ε = 8.93), and the dinuclear complex 2a AcOH are tabulated in Table 2.

complex	shell	CN ^a	$\sigma^{2b}/10^3 \text{ A}^{-2}$	$\Delta E_0^c/\mathrm{eV}$	$\Delta R^d/\text{\AA}$	$R_{\rm eff}^{\ e}/{ m \AA}$	<i>R^f∕</i> Å	$\chi_{\rm v}^{2g}$	R-factor
6a·2H₂O	Cu-O1/O3	4	5.6 ± 0.8	1.63 ± 1.41	-0.07	1.991	1.92 ± 0.01	171.6	0.0098
	Cu-C1	2	15.4 ± 14.0	6.34 ± 2.34	-0.07	2.679	2.61 ± 0.06		
	Cu-O2	2	15.4 ± 14.0	6.34 ± 2.34	0.13	2.682	2.81 ± 0.06		
$6a \cdot 2H_2O^h$	Cu-O1/O4	2	5.5 ± 0.8	4.23 ± 0.90	0.01	1.898	1.91 ± 0.09	151.1	0.0092
	Cu-O3/O6	2	5.5 ± 0.8	4.23 ± 0.90	0.01	1.940	1.95 ± 0.09		
	Cu-C1/C2	2	8.5 ± 5.0	-2.87 ± 10.98	-0.04	2.858	2.82 ± 0.09		
	Cu-O2/O5	2	8.5 ± 5.0	-2.87 ± 10.98	-0.04	3.180	3.14 ± 0.09		
2a·AcOH	Cu-O1/O2/O3	3	3.7 ± 0.7	7.61 ± 1.22	-0.02	1.957	1.94 ± 0.01	182.9	0.016
	Cu-O4	1	3.7 ± 0.7	7.61 ± 1.22	-0.01	2.0036 ± 19	1.99 ± 0.01		
	Cu-O5	1	3.7 ± 0.7	7.61 ± 1.22	-0.02	2.193 ± 0.005	2.17 ± 0.01		
	Cu1-Cu2	1	11.8 ± 7.7	7.61 ± 1.22	-0.14	2.5804 ± 0.014	2.44 ± 0.06		
	Cu1-C1/C2	2	13.6 ± 8.3	-0.84 ± 5.83	0.03	2.822	2.85 ± 0.11		
	Cu-C3	1	13.6 ± 8.3	-0.84 ± 5.83	0.03	2.845	2.88 ± 0.11		
	Cu-C4	1	13.6 ± 8.3	-0.84 ± 5.83	0.03	2.936	2.97 ± 0.11		
	Cu-O-C	6	13.6 ± 8.3	-0.84 ± 5.83			3.05 ± 0.11		
	Cu-O7	1	13.6 ± 8.3	-0.84 ± 5.83	-0.04	3.087	3.05 ± 0.11		
	Cu-O6/O8	2	13.6 ± 8.3	-0.84 ± 5.83	-0.01	3.095	3.09 ± 0.11		
	Cu-09	1	13.6 + 8.3	-0.84 + 5.83	0.00	3.189	3.19 + 0.11		

Table 2. *r*-Space-Based Metrical Parameters of FEFF Fitting Determined from the Crystal Structure of 6a·2H₂O, DFT-Optimized Structure of 6a·2H₂O, and the Dinuclear Complex 2a·AcOH

^{*a*}Co-ordination number. ^{*b*}Debye–Waller factor. ^{*c*}Measured energy shift. ^{*d*} $R - R_{eff}$. ^{*e*}Initial bond length for the scattering path based on single crystal XRD/DFT.^{*h*}*f*Bond length from FEFF fitting. ^{*g*}Reduced χ value. ^{*h*}Optimized structure calculated at the UB3LYP/6-31G(d,p) level of theory with a solvent effect.

The corresponding ball and stick models are demonstrated in Figure 6. The crystallographic structure of the mononuclear



Figure 6. Ball and stick models of $6a \cdot 2H_2O$ and $2a \cdot AcOH$ used for the determination of the atomic coordinates in the FEFF fitting with selected numbering schemes.

species $6a \cdot 2H_2O$ correlates with the solution-phase EXAFS spectrum following the catalysis starting from dinuclear $2a \cdot AcOH$ (*vide infra*). The *R* factor in the *r*-space, which is analogous to the confidence factor for single-crystal XRD in the range of 1.22 < r < 2.70 Å is less than 1% (0.0098), suggesting excellent coincidence. However, the crystallographic structure of $6a \cdot 2H_2O$ has a semi-infinite structure derived from

intermolecular hydrogen bonding that may affect the FEFF result. A stable structure of $6a \cdot 2H_2O$ was obtained by the DFT calculations, in which the OAc $-\kappa^1O$ coordination was stabilized by intramolecular hydrogen bonding with the aqua ligands giving a discrete structure (Figure 6). Such structural differences are reflected in the FEFF parameters in Table 2. In solution, $6a \cdot 2H_2O$ is expected to have the DFT-based structure rather than the X-ray structure. When the FEFF fitting was performed on the structure based on the DFT calculations, the degree of coincidence increased further, and the *R* factor in the *r*-space converged at 0.0092 (1.22 < *r* < 3.20 Å). Figure 7 demonstrates the FEFF-based EXAFS fitting analyses employing the atomic coordinates extracted from the optimized structural data for $6a \cdot 2H_2O$ by DFT calculations. Figure 7A shows the FEFF fitting analysis of the *k*-space.

In XAFS, because the radial distance obtained from the Fourier transformation is not always equal to the real one due to the phase problem,²¹ the analysis by the imaginary part was performed and showed a good coincidence (Figure 7B). Finally, based on our analysis, the FEFF evaluation strongly suggests that the catalytic solution predominately contains the mononuclear species $6a \cdot 2H_2O$ (Figure 7A–C). Conversely, under the same conditions as for $6a \cdot 2H_2O$, the FEFF fitting based on the dinuclear complex $2a \cdot AcOH$ diverged. Although the fitting was possible with calculations under looser fitting conditions (3 shells), the χ_v^2 value was larger than for $6a \cdot 2H_2O$ and the Cu–Cu bond converged at a longer length than the actual bond to achieve an acceptable fitting accuracy (Figure S9).

Screening Cu Catalysts for Dehydrogenative Coupling of Dimethyl Phthalate. With the spectroscopic evidence of the Cu complexes in hand, we screened the Cu catalysts for the dehydrogenative coupling of dimethyl phthalate under the standard catalytic conditions described above (Table 3). In the first instance, the screening was conducted with $2a \cdot H_2O$, as it has previously been used as a Cu catalyst,² and the complex $2a \cdot H_2O$ effectively afforded the



Figure 7. FEFF fitting analyses of the *k*-space of (A), the imaginary component in the *k*-space (B), and the *r*-space (C) of the EXAFS spectrum after catalysis starting from $2\mathbf{a} \cdot \mathbf{H}_2 O$ (black) and FEFF-fitting based on the optimized structure of $6\mathbf{a} \cdot 2\mathbf{H}_2 O$ (red) calculated at the UB3LYP/6-31G(d,n) level of theory including a solvent effect. The gray box indicates the calculation range for the *R* factor.

biaryl products (4/5 = 96/4) in 10.8% yield (TON of Cu = 139) (entry 1). [Cu(OAc)₂(phen)]·0.5H₂O (**2b**·0.5H₂O) also displayed good catalytic activity (entry 2), although an induction period was observed in the time-course curve.³ Notably, the catalysis barely proceeded in the absence of a Cu catalyst (entry 3), and was entirely inhibited when an excess amount of phen·H₂O was added to the catalytic system (entry 4). On the other hand, the monovalent Cu complex Cu(OAc) (**2c**) exhibited a high catalytic activity (entry 5). Interestingly, monovalent copper oxide (Cu₂O) was an optimal catalyst for

the reaction, while divalent copper oxide (CuO) was not (entries 6 and 7). Considering the carboxylate, Cu(OPiv)₂ displayed a high catalytic activity, whereas the electrondeficient Cu(OTf)₂ species proved to be a moderate catalyst (entries 8 and 9). It is noteworthy that Cu(OTf)₂ was an effective catalyst for the dehydrogenative coupling of *o*xylene.²² Finally, Cu(OH)₂, Cu(acac)₂, Cu(HFacac)₂, and Cu(I) and Cu(II) complexes exhibited a moderate to high catalytic activity (entries 10–20). What we learned from these experiments was that (i) a Cu catalyst was indispensable for the catalysis, (ii) coordination of phen to Cu inhibited the catalysis, and (iii) most Cu salts were catalytically active, regardless of the oxidation state.

Stoichiometric Reactions. The role of the Cu catalyst in the dehydrogenative coupling of dimethyl phthalate (3) was generally believed to involve the re-oxidation of the Pd(0) intermediate **1e**, which was produced by a reductive elimination of bis(dimethyl-3,4-phtharyl)palladium(II) complex **1d** (Scheme 1). However, to the best of our knowledge, no such stoichiometric reaction has been reported so far. When a zerovalent Pd complex [Pd(dba)(phen)] (7)²³ was treated with 2 equiv of Cu(OAc)₂·H₂O (**2a**·H₂O) at 60 °C for 3 h under a N₂ atmosphere, a bis(acetato)palladium(II) complex [Pd(OAc)₂(phen)] (**1b**) was obtained as a yellow crystalline powder in 88–95% yield (eq 2).



A similar treatment using 1 equiv of $2a \cdot H_2O$ also gave 1b; however, the product yield decreased to 56-63%. This is the first clear evidence of the regeneration of 1b from a Pd(0) species by 2a. According to this result, the reaction stoichiometry of 7 and $2a \cdot H_2O$ is presumably 1 to 2. Moreover, the characterization of the fate of 2a in this reaction proved to be challenging. Nonetheless, acetatocopper-(I) species is a conceivable product. The potential mechanism involves an acetato group transfer through the "Pd(μ^2 -OAc)Cu" species. It is noteworthy that a related "Pd(μ^2 -O₂C^tBu)Cu" complex [trans-(picoline)₂Pd(O₂C^tBu- μ^2 -Pd,Cu)₂Cu₂(O₂C^tBu- μ^2 -Cu,Cu')₄] has been isolated.²⁴

To study the re-oxidation step of the monovalent Cu species to a divalent species, the monovalent complex 2c was refluxed for 1.5 h in AcOH in air. Pleasingly, $[Cu(OAc)_2]_2$ ·2AcOH (2a· AcOH) was selectively obtained as blue cubic crystals in 90% yield. The molecular structure was unambiguously characterized by single-crystal XRD (eq 3).

The molecular structure of $2a \cdot AcOH$ is essentially identical to the corresponding dimer $2a \cdot H_2O$. The species exhibits a paddle wheel dinuclear structure capped with two molecules of AcOH (Figure 8). The molecular structure of $2a \cdot AcOH$ was previously reported by Manohar and co-workers, who obtained the single crystals by a simple recrystallization of the

Table 3. Screening of Cu Catalysts for the Dehydrogenative Coupling of Dimethyl Phthalate



	MeO ₂ O	4	5			
		3	dimers		TC	0N ^a
Entry	Cu catalyst	conv./% ^a	yield/% ^a	4/5	Pd	Cu
1	$Cu(OAc)_2 \cdot H_2O$	12.8	10.8	94/6	83	139
2	[Cu(OAc) ₂ (phen)]·0.5H ₂ O	13.5	10.5	94/6	81	136
3	None	3.2	1.3	94/6	10	n.d.
4 ^b	$Cu(OAc)_2 \cdot H_2O$	4.3	n.d.	n.d.	n.d.	n.d.
5	Cu(OAc)	14.5	10.7	94/6	83	138
6	Cu ₂ O	11.7	9.4	94/6	73	133
7	CuO	4.2	1.5	94/6	12	20
8	$Cu(OPiv)_2^c$	13.0	10.9	94/6	84	140
9	$Cu(OTf)_2^d$	6.7	5.0	87/13	39	65
10	$Cu(OH)_2$	12.2	9.5	93/7	74	123
11	$Cu(acac)_2^e$	12.8	9.3	93/7	72	126
12	Cu(HFacac) ₂ ^f	14.2	10.8	94/6	84	140
13	CuCN	6.8	5.5	95/5	43	70
14	CuSCN	10.2	8.7	94/6	68	113
15	CuTC ^g	11.2	9.7	94/6	75	124
16	CuCl ₂	11.8	8.7	95/5	67	112
17	CuBr ₂	8.0	7.1	95/5	55	91
18	CuCl	9.9	8.3	94/6	64	108
19	CuBr	10.1	8.7	95/5	67	111
20	CuI	8.6	8.3	94/6	64	107

^{*a*}Conditions; [1b] = 4.00 mM (0.0653 mol %), [Cu] = 1.20 mM (0.0196 mol %), 3: 25 mL, air bubbling (0.1 MPa), 200 °C, 6 h. Conversion, GC yield of dimers, and TON were indicated as the average of three runs. ^{*b*}[phen] = 26.0 mM. ^{*c*}OPiv = pivalate. ^{*d*}OTf = trifluoromethanesulfonyl. ^{*c*}acac = acetylacetonato. ^{*f*}HFacac = hexafluoroacetylacetonato. ^{*g*}TC = thiophenecarboxylato.



Figure 8. Molecular structure of a dimer of $[Cu(OAc)_2]_2$ ·2AcOH (**2a**·AcOH) by single crystal XRD. Cu (yellow), O (red), and C (black). All hydrogen atoms are omitted for clarity. Ellipsoids represent 50% probability.

dehydrated powder of 2a from a mixture of acetic acid/acetic anhydride (3/1).²⁵ We illustrated the molecular structure of 2a·AcOH, as it provides solid evidence for the formation of the divalent species 2a from a monovalent complex 2c. The

selected crystallographic data and bond lengths for 2a·AcOH are listed in Table 4. The crystallographic data for 2a·AcOH

Table 4. Selected Crystallographic Data and Bond Lengths (Å) for [Cu(OAc)₂]₂·2AcOH (2a·AcOH)

chemical formula	$C_6H_{10}CuO_6$					
formula weight	241.69	241.69				
crystal system	monoclinic	monoclinic				
space group	$P2_1/n$ (no. 14)					
Ζ	4					
R(wR)	0.0473 (0.1227)					
GOF	1.128					
Cu-O	1.952(2)	1.956(2)				
	1.962(2)	2.0036(19)				
	2.193(2)					
Cu–Cu	2.5804(14)					

obtained in the current study are in agreement with Manohar's report. Although the hydrogen atoms in the coordinated AcOH molecule are not shown in Figure 6, they were determined to be oriented toward the oxygen atom in one of the μ -AcO moieties, suggesting the presence of intramolecular hydrogen bonding.

Discussion on the Mechanism. Based on the mechanistic studies involving the solution-phase XAFS analysis as well as the evaluation of the catalytic and stoichiometric reactions, in Scheme 2, we propose a Cu cycle for the catalytic

Scheme 2. Proposed Mechanism for the Dehydrogenative Coupling of Dimethyl Phthalate Catalyzed by $[Pd(OAc)_2]/Cu(OAc)_2/phen$



dehydrogenative coupling of dimethyl phthalate. Namely, the $Cu(OAc)_2$ species oxidizes the Pd(0) species "Pd(phen)" le to regenerate $[Pd(OAc)_2(phen)]$ (1b), as demonstrated in the stoichiometric reaction. On the other hand, the $Cu(OAc)_2$ species is suspected to be converted to the monovalent Cu(OAc) species. Subsequently, re-oxidation of Cu(OAc) with AcOH in air gives 2a·AcOH. Notably, the monovalent Cu complex 2c also affords a divalent Cu complex 2a. Although this process is not well understood, it is considered that this process is a disproportionation reaction because the reaction proceeds in the absence of AcOH. As mentioned above, a dinuclear paddle wheel was originally proposed as the structure of 2a. However, the EXAFS data obtained in the current study suggest that the intermediate (or resting state) is a mononuclear Cu(II) species, most likely 6a·2H₂O, although the presence of a minor dimeric species cannot be excluded. The conversion from a dinuclear $[Cu(OAc)_2]_2 \cdot 2L$ (2a·L: L = H_2O or AcOH) to a mononuclear $[Cu(OAc)_2]$ species was well characterized, and the transformation to mononuclear complexes was determined to be triggered by the removal of the axial ligand. For example, Sharrock and Melnik reported that in the case of $[Cu(OAc)_2]_2$ ·2AcOH (2a·AcOH), the axial acetic acid ligand was lost even at temperatures as low as 40 °C, which was estimated by thermogravimetric analysis. The process eventually yielded a mononuclear $[Cu(OAc)_2]$ species.²⁶ Furthermore, Kochi and Subramanian evaluated the equilibrium constant between the dimeric and monomeric $[Cu(OAc)_2]$ in glacial acetic acid: $K = 5.8 \pm 0.3 \times 10^{-4}$ M at 57 °C, which corresponds to 30% dissociation of the dimer at 2 $\times 10^{-3}$ M of $[Cu(OAc)_2]$.²⁷ Further studies are necessary to

establish how the present catalytic system stabilizes the monomeric "Cu(OAc)₂" species.^{28,29} Because the dehydrogenative arene coupling produces water as the side product, the formation of a bis(aqua) adduct is suspected to contribute to the stabilization of the monomeric form.¹⁵ In some cases of the Wacker type reaction using PdCl₂ and CuCl₂, the *in situ* formation of a Pd–Cu dinuclear complex has been proposed.^{5,30} However, the results of our study do not support the formation of a heterodinuclear species bearing a direct Pd–Cu bond.

The phen ligand readily coordinates with 2a to give 2b, which does not work with the described catalysis. According to our previous study,³ the free phen moiety rapidly coordinates with 2a in a dimethyl phthalate solution, while the spontaneous ligand migration from $[Pd(OAc)_2(phen)]$ (1b) to 2a is very limited.

The involvement of the dioxygen copper species in the described catalytic process is also noteworthy. There have been extensive investigations on and evidence for the presence of dioxygen complexes of Cu as well as for application of 2a as an oxidant in air.³¹ Notably, the present results cannot rule out the *in situ* formation of these dioxygen copper complexes. The oxidation step of the Pd(0) complex presumably involves 2 equiv of 2a, as shown in eq 2. We also believe that 2a or the dioxygen product is not involved in the C-H bond cleavage step of dimethyl phthalate. This is because $[Pd(OAc)_2L]$ cleaves an aromatic C-H bond,³² and our previous study on the microscopic reversibility³ supports the linkage between 1b and 1c. The outcomes of the current work demonstrate that two equiv of $6a \cdot 2H_2O$ results in the oxidation of Pd(0), with subsequent regeneration of $6a \cdot 2H_2O$ from $6c \cdot 2H_2O$ in the presence of AcOH in air. We therefore conclude the Cu cycle mechanism, as illustrated in Scheme 2. Although the Cu cycle involving a dimeric species cannot be completely ruled out, the described EXAFS studies and the presence of an equilibrium mixture between the dimeric and monomeric $Cu(OAc)_2$ species support the established catalytic cycle.

According to this study, we can also draw the conclusions that (i) $2\mathbf{a}\cdot H_2O$, $2\mathbf{c}$, and $2\mathbf{b}\cdot 0.5H_2O$ were considered to give $6\mathbf{a}\cdot 2H_2O$, (ii) $2\mathbf{c}$ was converted to $2\mathbf{a}\cdot H_2O$, and (iii) $2\mathbf{b}\cdot 0.5H_2O$ was prepared from $2\mathbf{a}\cdot H_2O$ based on the literature method.³³ These facts explain the behavior outside the Cu cycle in Scheme 2.

Concluding Remarks. The detailed mechanism of the Pd/ Cu-catalyzed dehydrogenative coupling of dimethyl phthalate has been the subject of long-standing discussion. The described XAFS studies, FEFF analyses, as well as evaluation of the catalytic and stoichiometric reactions allowed for the establishment and proposal of the Cu cycle. Based on our previous study on the Pd cycle,³ the present work now revealed the entire mechanism of the Pd/Cu-catalyzed dehydrogenative coupling of 3 and the catalytically active species in the Cu cycle to be $[Cu(OAc)_2] \cdot 2H_2O$ (6a $\cdot 2H_2O$). The clarified mechanism of the Cu cycle is analogous to the previously proposed one. Nevertheless, it is crucial to provide valuable evidence supporting the mechanism through various experimental studies. An interesting finding is the importance of the phen ligand for the Pd catalyst; however, it was shown that the ligand suppresses the activity of the Cu catalyst. Thus, the present study recommends utilizing [Pd(OAc)₂(phen)] (1b) as the Pd catalyst instead of the addition of phen to the $[Pd(OAc)_2]$ (1a)/Cu(OAc)₂ system.

EXPERIMENTAL SECTION

General Procedures. All procedures described in this paper were carried out in air, unless stated otherwise. $Cu(OAc)_2 \cdot H_2O$ (2a·H₂O), Cu(OAc) (2c), Cu_2O , CuO, Cu(OPiv)₂, Cu(OTf)₂, Cu(OH)₂, Cu(acac)₂, Cu(HFacac)₂, CuCN, CuSCN, CuTC, CuCl₂, CuBr₂, CuCl, CuBr, and CuI were purchased from commercial suppliers and used as received. $[Pd(OAc)_2(phen)]$,³³ $[Pd(dba)_2]$,³⁴ $[Pd(dba)_2]$ (phen)],²² and $[Cu(OAc)_2(\text{phen})] \cdot 0.5H_2O$ (**2b** $\cdot 0.5H_2O$)³⁵ were prepared according to literature methods. ¹H and ¹³C{¹H} nuclear magnetic resonance (NMR) spectra were recorded on a JEOL ECX-400P instrument (400 MHz for ¹H). Chemical shifts (δ) are given in ppm, relative to tetramethylsilane. All coupling constants are given in Hz. Infrared spectra were recorded on a JASCO FT/IR-4100 instrument with the use of KBr disks. GLC analyses were performed on a Shimadzu GC-14B instrument with an FID detector equipped with an InertCap 1 column (0.25 mm i.d. × 30 m). The catalytic reactions were carried out using an EYELA SynFlex aluminum brock heater.

Solution-Phase XAFS Measurements. Cu K-edge XANES and EXAFS measurements were carried out at the BL01B1 beamline at SPring-8 of the Japan Synchrotron Radiation Research Institute (JASRI). All measurements were performed at room temperature. The Cu K-edge XAFS data were recorded in the fluorescent mode. The X-ray energy was calibrated using a Cu foil, and the data analyses were performed utilizing ATHENA in the Demeter software package for Windows (ver. 0.9.26).¹⁷ For the solution-phase XAFS, the catalyst solution in dimethyl phthalate (3) employed as the solvent was filtered through a PTFE membrane filter of 0.2 μ m pore size, and a portion of the resulting solution (ca. 1 mL) was sealed in a plastic bag (Seinichi Unipack S-4: 55 mm \times 40 mm \times 0.04 mm). The sealed plastic bag was secured in a plastic slide mount (Hosho slide mount, outside size: 50 mm × 50 mm, window size: 34 mm \times 23 mm) for XAFS study.

XAFS Study of Cu Complexes in Dimethyl Phthalate. 2a·H₂O (37.4 mg, 0.187 mmol), 3 (25 mL), and a magnetic stirrer bar were placed in a 50 mL vial. The reaction system was heated at 120 °C until its color changed to brown. The solution (1 mL) was filtered through a PTFE membrane, and the filtrate was transferred to a plastic bag before carrying out the XAFS measurements.

XAFS Study of the Catalytic Solution. The catalytic solution for the XAFS study was prepared and performed as summarized in Table 1.

Catalytic Dehydrogenative Coupling of Dimethyl Phthalate. [Pd(OAc)₂(phen)] (1a; 40.47 mg, 0.1000 mmol), Cu(OAc)₂·H₂O (2a·H₂O; 5.98 mg, 0.0300 mmol), dimethyl phthalate (3; 25.0 mL, 150.0 mmol), and a magnetic stirrer bar were placed in a four-necked round-bottom flask. Subsequently, a reflux condenser, the gas inlet, a thermometer, and a stopper were installed on the flask. A stream of air was passed through the solution by means of a mini-compressor, and the reaction system was heated at 200 °C for 6 h with magnetic stirring at a rate of 820 rpm. A portion of the solution ($500 \ \mu$ L) was transferred using a hypodermic syringe to a vial. Triphenylmethane as an internal standard (approx. 1 mmol) and THF (170 μ L) were added to the vial. The product yield and conversion were estimated by GLC analysis.

Stoichiometric Reaction of [Pd(dba)(phen)] (7) with Cu(OAc)₂·H₂O (2a·H₂O). Complex 7 (41.9 mg, 0.0804 mmol), 2a·H₂O (32.16 mg, 0.1600 mmol), and a stirrer bar were placed in a Schlenk tube (25 mL) under a N₂ atmosphere. Dry benzene (5.4 mL) was introduced into the tube using a hypodermic syringe. The reaction mixture was warmed at 60 °C for 3 h. A change of color from dark brown to yellow or amber was noted. After cooling to room temperature, the insoluble materials were removed by centrifugation. The residue was washed with benzene $(5 \times 5 \text{ mL})$ and extracted with dichloromethane (DCM, 5 mL) using ultrasonic irradiation. The subsequent centrifugation gave a yellow solution. The extraction process was repeated 7 times. The combined yellow solution was filtered through a cannula with a glass filter. All volatile solvents and compounds were removed using a rotary evaporator, and the resulting solid was dried under vacuum. The obtained yellow powder was confirmed as $[Pd(OAc)_2(phen)]$ (1b) by ¹H NMR spectroscopy. Yellow microcrystals, 31.0 mg (0.0767 mmol), 95% yield. The 2nd trial of this process conducted under the same conditions also gave 1b in 88% yield. A similar treatment of 6 (65.8 mg, 0.126 mmol) with 2a·H₂O (25.20 mg, 0.1262 mmol) gave 1b in 56% yield. Finally, the 2nd trial of the reaction of 7 with $2a \cdot H_2O$ in a 1/1 ratio gave 1b in 63% yield.

Stoichiometric Reaction of Cu(OAc) (2c) with AcOH. 2c (150.07 mg, 1.2242 mmol), AcOH (7 mL), and a magnetic stirrer bar were placed in an eggplant flask. Subsequently, a reflux condenser was installed on the flask. The reaction system was heated at 135 °C for 1.5 h under magnetic stirring. The hot solution was filtered using a cannula with a glass filter. The solution was allowed to cool at room temperature and the deposition of deep blue cubic crystals was noted. The cubic crystals were washed with hexane (3×5 mL). Further crystals were obtained from the mother liquors and were treated analogously. The combined crystals of **2a**·AcOH were dried under reduced pressure. The total yield of **2a**·AcOH was determined at 90% (265.2 mg, 1.09 mmol). This compound was identified as 7 by single-crystal X-ray structure analysis.

Single-Crystal X-ray Structure Analysis. Single crystals of 7 were selected using a polarized optical microscope. A selected single-crystal suitable for single-crystal X-ray structure analysis was mounted on top of a glass capillary using Paratone N oil. A Rigaku AFC-7R Mercury II diffractometer with graphite-monochromated Mo K α radiation ($\lambda = 0.71075$ Å) was used for data collection at 293 K. The collected data were solved by direct methods (SHELXL ver. 2018/1)³⁶ and refined by a full-matrix least-squares procedure employing the Crystal Structure program (ver. 4.3).³⁷ All hydrogen atoms were treated as a riding model. The POV-Ray program (ver. 3.6.2) was used for depiction of the molecules.³⁸ CCDC 1963800 contains the supplementary crystallographic data for 2a AcOH. These data can be obtained free of charge via http://www. ccdc.cam.uk/conts/retrieving.html, or from Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB2, 1EZ, UK; fax (+44) 1223-336-033; or e-mail deposit@ccdc. cam.ac.uk.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acscatal.0c00918.

Spectroscopic and physical data and detailed FEFF fitting data (PDF)

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Notes

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ABBREVIATIONS

DBA, dibenzylidene acetone $(C_{17}H_{14}O)$; DCM, dichloromethane (CH_2Cl_2) ; phen, 1,10-phenanthroline $(C_{12}H_8N_2)$; THF, tetrahydrofuran (C_4H_8O)

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