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Mechanistic Insight into the Copper-Catalyzed Phosphorylation of Terminal Alkynes: A Combined Theoretical and Experimental Study

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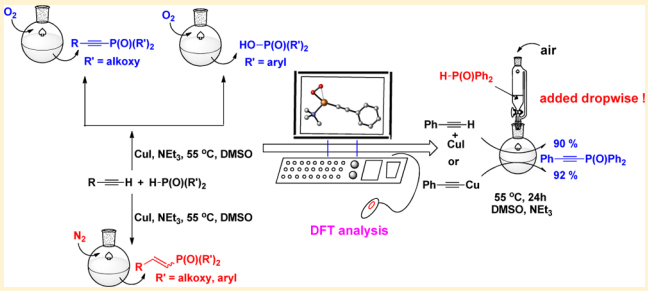
Supporting Information

ABSTRACT: The reaction mechanism of copper-catalyzed phosphorylation of terminal alkynes under different conditions has been investigated experimentally and theoretically. The important role of dioxygen has been elucidated, including the formation of η^1-superoxocopper(II), η^2-superoxocopper(III), μ-η^2:η^2-peroxodicopper(II), and bis(μ-oxo)dicopper(III) complexes. More importantly, the proton transfer from the dialkyl phosphonate (in the form of phosphite) to the bridging oxygen atom entails the migration of the deprotonated phosphonate to the terminal alkyne, leading to the formation of a C−P bond with an activation barrier of only 1.8 kcal/mol. In addition, a particularly stable six-centered dicopper(I) species is formed with the migration of both of the $Ph_2P(O)$ groups from the copper atoms to the oxygen atoms of the bis(μ-oxo) bridge, explaining the experimental observation that secondary phosphine oxides can be oxidized to the phosphinic acids. Thus, the diphenylphosphine oxide was added to the reaction mixture dropwise to minimize the concentration during the reaction course. Gratifyingly, the coupling product was generated almost quantitatively when the reaction was completed.

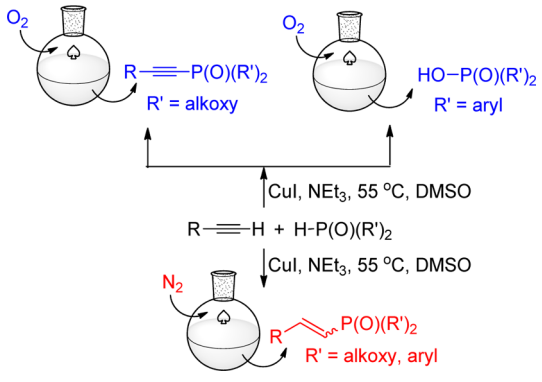


1. INTRODUCTION

Organophosphorus compounds play a crucial role in pharmaceutical and agrochemical industries. The presence of a phosphoryl group often significantly improves the hydrophilicity and bioavailability.[1] In particular, alkynyl- and alkenylphosphorus compounds, which contain extremely versatile multiple bonds, can readily undergo nucleophilic addition to give bifunctional adducts.[2] Some of them have successfully been used as the precursors of biologically active molecules.[3]

In the past 10 years, a number of other metal-catalyzed oxidative couplings using dioxygen have been successfully applied to the construction of structurally sophisticated compounds.[4] For example, Stahl and co-workers reported copper-catalyzed chemoselective aerobic oxidation of alcohols[4a,b] and functionalization of an arene C−H bond.[4c] Dioxygen is undoubtedly the most environmentally benign and abundant oxidant because only water is produced as a byproduct.[5] We recently reported a copper-catalyzed aerobic oxidative cross-coupling of dialkyl phosphonates with terminal alkynes to provide a variety of alkynylphosphorus compounds.[6a] It is very interesting to note that alkynylphosphonates (Scheme 1 top, R′ = alkoxy) were formed in high yields in the presence of oxygen, while alkenylphosphorus compounds (Scheme 1 bottom, R′ = alkoxy or aryl) were generated under nitrogen.[6] Unfortunately,

Scheme 1. Copper-Catalyzed Phosphorylation of Terminal Alkynes under Oxygen or Nitrogen



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diarylphosphine oxides were found to be unsuitable coupling partners since they could be oxidized to the phosphinic acids (Scheme 1 top, R′ = aryl).[6a] Although copper-catalyzed oxidative couplings have attracted more and more attention,[5] the mechanism (e.g., the role of dioxygen) is not well understood.[5,7] Here, our continued interest in organophosphorus chemistry and reaction mechanisms[8] prompted us to investigate the detailed catalytic steps both experimentally and theoretically to probe the origin of the different behaviors summarized in Scheme 1. Benefiting from the theoretical findings, diphenylphosphine oxide was added dropwise to the reaction mixture under air, leading to the diphenyl(alkynyl)-phosphine oxide in excellent yield.

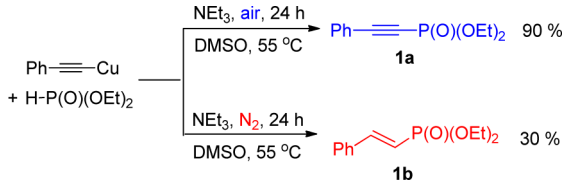
2. COMPUTATIONAL DETAILS

Optimizations of structures with frequency calculations were performed with the Gaussian 03 software package.[9a] Density functional theory (DFT) with the B3LYP functional,[10] which has been chosen in several mechanistic studies on Cu-catalyzed reactions,[11] and a mixed basis set employing D95v(d)[12] for C, H, N, and O and LANL2DZ[13] for P, I, and Cu was used. Polarization functions were added for P (ξ_d = 0.387), I (ξ_d = 0.289), and Cu (ξ_f = 3.525).[14] Transition states with only one imaginary frequency were examined by vibrational analysis and then submitted to intrinsic reaction coordinate (IRC) calculations to ensure that such structures indeed connected two minima. Energies in solution (DMSO) were calculated with the Gaussian 09 program[9b] by means of single-point calculations (IEF-PCM method with the Bondi radii)[15] with the same functional using the SDD[16] pseudopotential for I and Cu and the extended 6-311++G(2d,p)[17] basis set for the other atoms. The gas-phase geometry was used for all of the solution-phase calculations. A similar treatment was also used in many recent computational studies.[18] Dispersion corrections were computed for the optimized geometries using the DFT-D3 package of Grimme[19] with the corresponding B3LYP-D functional. The free energy correction from the frequency calculation and the dispersion correction were added to the single-point energy to obtain the free energy in solution. All of the solution-phase free energies reported herein correspond to the reference state of 1 mol/L, 298 K. In the calculations, the model substrates $(NMe_3)_2CuI$, dimethyl phosphonate, phenylacetylene, and dioxygen were chosen. Relative free energies in solution (DMSO) were employed to analyze the reaction mechanism. A comparison of some relative energy values of the reaction mechanism obtained with the model substrates [$(NMe_3)_2CuI$ and dimethyl phosphonate] and the real substrates [$(NEt_3)_2CuI$, diethyl phosphonate] is provided in the Supporting Information. The results show that the energies in the rate-determining steps did not differ significantly. For example, with the model substrates, the energies of **TS3** (relative to **IN6**) and **TS9** (relative to **IN16**) were 9.3 and 34.1 kcal/mol, respectively. With the real substrates, the relative energies were 8.6 and 32.8 kcal/mol, respectively. In addition, considering that the B3LYP functional is problematic in treating some transition-metal systems, we evaluated the effects of the density functional in this study. The results show that different DFT methods provided consistent energy profiles (for details, see the Supporting Information). Optimized structures were visualized using the CYLview program[20] and are provided in the Supporting Information.

3. RESULTS AND DISCUSSION

3.1. Cu-Catalyzed Dioxygen-Triggered Phosphorylation. Under air or nitrogen, phenylacetylene (0.3 mmol) and $(EtO)_2P(O)H$ (0.25 mmol) were added to a mixture of CuI (0.025 mmol) and NEt_3 (0.05 mmol) in DMSO to immediately give a yellow suspension, clearly demonstrating that (phenylethynyl)copper was formed.[21] Thus, the reaction may start when the alkyne and a base react with the copper catalyst, generating the alkynylcopper reagent. To examine our hypothesis, we treated (phenylethynyl)copper (0.3 mmol), NEt_3 (0.6 mmol), and $(EtO)_2P(O)H$ (0.25 mmol) in DMSO without the presence of CuI at 55 °C for 24 h (Scheme 2). Gratifyingly, the corresponding products diethyl (phenylethynyl)phosphonate (**1a**) and diethyl styrylphosphonate (**1b**) were formed under air and nitrogen, respectively.[22]

Scheme 2. Phosphorylation of (Phenylethynyl)copper



The catalytic cycle of the Cu-catalyzed dioxygen-triggered phosphorylation of terminal alkynes, including the free energies for all the species, is depicted in Figure 1, in which the Cu atoms have been color-coded to indicate the different oxidation states [Cu(I) is shown in black, Cu(II) in blue, and Cu(III) in red]. (Phenylethynyl)copper complex **IN1** (3.3 kcal/mol) is initially formed through a base-mediated ligand exchange process. Subsequently, reaction of dioxygen in the triplet state with **IN1** leads to the formation of the η^1-superoxocopper(II) intermediate **IN3** (triplet, 7.2 kcal/mol) via the low-barrier transition state **TS1** (8.4 kcal/mol). The Mulliken spin densities for **IN3** are mainly localized in the O_2 part (1.53), indicating that the oxidation state of the Cu center is +2. Interestingly, the Cu−O1 and Cu−O2 distances are 1.981 and 2.232 Å, respectively, in triplet-state **IN3**, while they are quite short (1.868 and 1.873 Å, respectively) in singlet-state **IN4** (16.2 kcal/mol) (Figure 2). This process (**IN3** → **IN4**) is expected to require a low activation energy.[5,23] When another **IN1** or **IN2** comes, the μ-η^2:η^2-peroxodicopper(II) intermediate **IN6** with a positive energy of 17.3 kcal/mol is formed via the three-membered transition state **TS2** (20.5 kcal/mol).

From **IN6**, the bis(μ-oxo)dicopper(III) complex **IN7** (12.9 kcal/mol) is formed through the four-centered transition state **TS3** with a one-electron transfer from each Cu(II) to the peroxo group. The activation energy was computed to be 9.3 kcal/mol. The O−O bond distances in **IN6** (peroxo) and **IN7** (oxo) are 1.429 and 2.313 Å, respectively, in line with experimental observations for similar species (1.42 and 2.32 Å, respectively).[23c]

It is well-known that for dialkyl phosphonates or secondary phosphine oxides in solution, a tautomeric equilibrium between a normal tetracoordinated form and an "active" tricoordinated one exists.[24] Both dialkyl phosphonates and secondary phosphine oxides favor the tetracoordinated form. The formation of a phosphorus−metal bond is the driving force for the tautomerization. Actually, the phosphite−copper(III) complex **IN9** (14.0 kcal/mol) is formed when dimethyl phosphonate (via the form of dimethyl hydrogen phosphite) coordinates to **IN7**. Very interestingly, the more stable intermediate **IN10** (−34.1 kcal/mol) is formed through **TS5** with an activation energy of 1.8 kcal/mol in a process featuring not only a proton transfer from P−O−H to Cu−O_2−Cu but also the spontaneous formation of a P−C bond; a more stable intermediate, **IN11** (−40.7 kcal/mol), can subsequently be generated via a hydrogen-bond-like interaction of a second dimethyl hydrogen phosphite. It is important to note that several Cu_2O_2 species are proposed as a mixed-valence Cu(III)/Cu(I) core.[25] Indeed, in **IN10** the Cu3−OH bond

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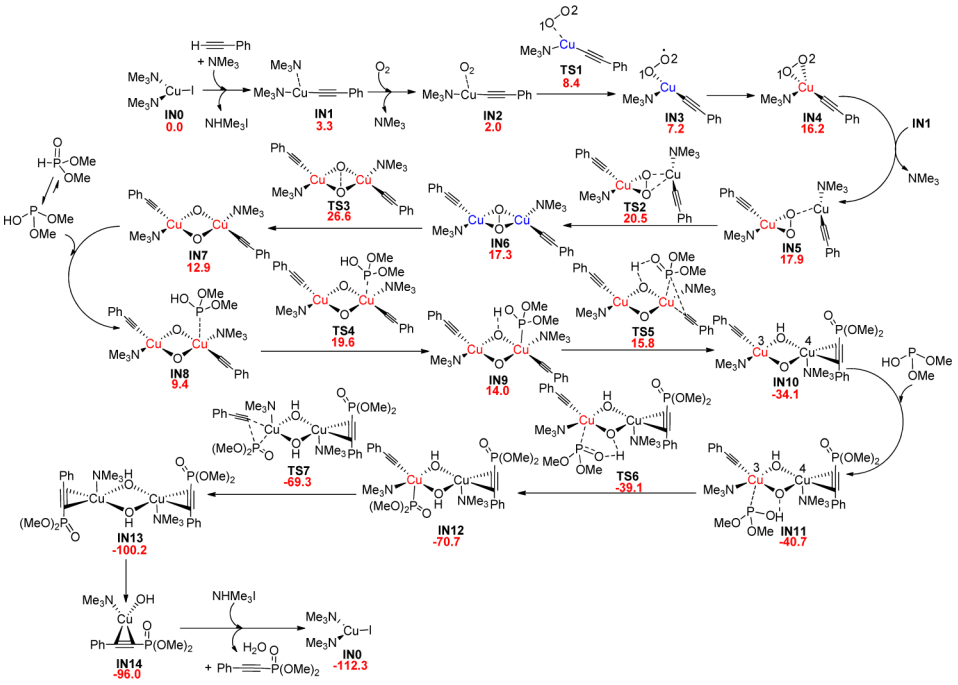

Figure 1. Free energy profile for the copper-catalyzed dioxygen-triggered phosphorylation of terminal alkynes. Free energy values in kcal/mol are shown in red.

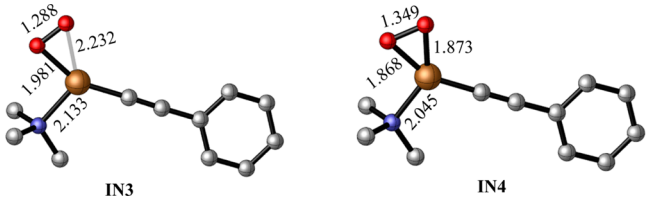

Figure 2. Structures of singlet **IN3** and triplet **IN4**. H atoms have been omitted for clarity. Distances in Å are shown.

(1.851 Å) is much shorter than Cu4−OH bond (2.386 Å), clearly indicating that the Cu4−OH bond is a weak coordinate bond and thus the oxidation states of Cu3 and Cu4 are +3 and +1, respectively, similar to other Cu(III)/Cu(I) species.

Subsequently, the five-membered transition state **TS6** appears to be only 1.6 kcal/mol higher than **IN11**, leading to the formation of a more stable species **IN12** (−70.7 kcal/mol). From **IN12**, a three-centered transition state **TS7** with an activation energy of 1.4 kcal/mol was located. In **TS7**, the Cu−C, Cu−P, and C−P bond lengths are 1.863, 2.314, and 2.446 Å, respectively. In comparison with our previous study on the C−P bond formation step using a palladium(II)[8a] or nickel(II)[2i,8e,i] catalyst, this C−P bond is quite long, indicating that the Cu(III) species is a potentially useful catalyst for the transformation.

Then the dinuclear intermediate **IN13** breaks up into two monomeric copper(I) species (**IN14**). Finally, ligand exchange gives the desired product (−112.3 kcal/mol) and completes the catalytic cycle by regenerating **IN0** as a catalytically active species. Comparing the steps of the copper-catalyzed dioxygen-triggered phosphorylation, one could conclude that cleavage of the O−O bond is the overall rate-limiting step. The barrier is 26.6 kcal/mol with respect to the catalyst resting state **IN0**, in excellent agreement with the experimental observations that this reaction was performed at 55 °C.[26]

3.2. Cu-Catalyzed Dioxygen-Free Phosphorylation. Under similar conditions, alkenylphosphorus compounds were generated under nitrogen (Schemes 1 and 2).[6] As

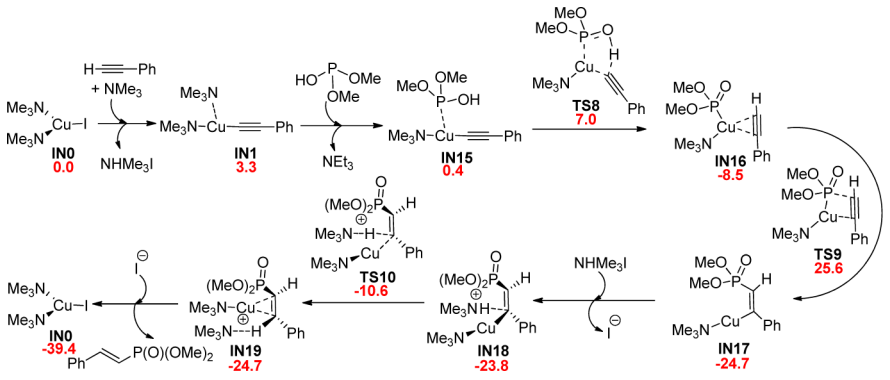

Figure 3. Free energy profile for the copper-catalyzed phosphorylation of terminal alkynes under nitrogen. Free energy values in kcal/mol are shown in red.

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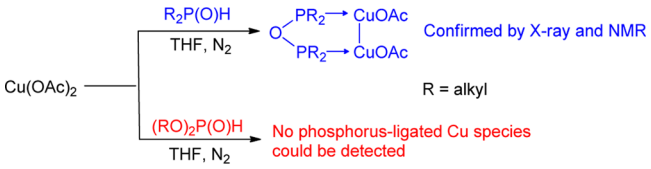
shown in Figure 3, this catalytic cycle includes four basic steps: ligand exchange, proton transfer, nucleophilic addition, and catalyst recycling. Our calculations showed that the addition step is the most energy-demanding. The activation barrier was computed to be 34.1 kcal/mol, which is much higher than that of dioxygen-triggered process. Although the regeneration of the catalytically active species **IN0** is exoergic by −39.4 kcal/mol, it is much less exoergic than that of dioxygen-triggered process (−112.3 kcal/mol). Thus, dioxygen-free phosphorylation is not favorable either kinetically or thermodynamically. Indeed, only a 30% yield of (*E*)-diethyl styrylphosphonate was obtained after 24 h, along with 70% unchanged reactant (Scheme 2).

3.3. Oxidation of Secondary Phosphine Oxides and Dialkyl Phosphonates. Unfortunately, secondary phosphine oxides such as $Ph_2P(O)H$ did not provide the oxidative coupling product under similar reaction conditions. Only $Ph_2P(O)OH$ was detected in the crude mixture.[6a] Drawing inspiration from our experience in organophosphorus chemistry, we found that the copper catalyst is susceptible to secondary phosphine oxides rather than dialkyl phosphonates (Scheme 3).[8j] Actually, the energy of the HOMO in tricoordinated Ph_2POH is 0.02 eV higher than that in $(MeO)_2POH$, and thus, Ph_2POH is more nucleophilic. The energy of the LUMO in $(MeO)_2POH$ is 0.03 eV, whereas that in Ph_2POH is −0.03 eV, indicating that Ph_2POH is also a better candidate for enhancing back-donation from the Cu center.[27] Hence, we presume that tricoordinated phosphine could strongly bind to the Cu center using its lone electron pair, inhibiting the in situ formation of alkynylcopper and instead forming the phosphine−copper complex, where the phosphorus(III) center might be easily oxidized by dioxygen.

Scheme 3. Previous Study of Coordination Ability Using Secondary Phosphine Oxides and Dialkyl Phosphonates (R = Alkyl)



A possible mechanism is proposed on the basis of the above analysis (Figure 4). A more stable intermediate, **IN20** (−5.7 kcal/mol), is formed via a ligand replacement process. In a similar way, after two steps, the μ-η^2:η^2-peroxodicopper(II) complex **IN22** (−8.7 kcal/mol) is generated. Very interestingly, upon cleavage of the O−O bond in **IN22**, no bis(μ-oxo)dicopper(III) complex could be located. Instead, the very stable six-centered dicopper(I) species **IN23** (−155.7 kcal/mol) is formed with the migration of both of the $Ph_2P(O)$ groups from the copper atoms to the oxygen atoms of the bis(μ-oxo) bridge. It should be noted that this process is strongly exergonic because the transition state (**TS11**) appears with a one-electron transfer from each Cu to the peroxo group so that the oxidation states of Cu have been increased to +3. However, the corresponding dicopper(III) species is not stable enough to be found, indicating that in this case the $Ph_2P^{III}(O)$ group is very easily oxidized to the $Ph_2P^{V}(O)O$ group, in line with the experimental observation that only the oxidized product (phosphinic acid) was detected.

Since a side product, $(i\text{-PrO})_2P(O)OH$, was detectable in 3% yield,[6a] we next turned our attention to the oxidation of dialkyl phosphonates (see the Supporting Information for details). Our calculation results show that the formation of intermediate **IN21′** (8.3 kcal/mol) is unfavorable relative to **IN3** (7.2 kcal/mol). Although the energy difference is not significant, the (phenylethynyl)copper complex is regarded as a slightly soluble coordination polymer with strong π bonding between the metal and the acetylenes,[28] promoting a forward shift in the chemical equilibrium toward **IN3**.

3.4. Synthesis of Diphenyl(alkynyl)phosphine Oxides. On the basis of above calculation results, once the tricoordinated phosphine binds to the Cu center, the in situ formation of alkynylcopper might be inhibited. In addition, the phosphine is readily oxidized by dioxygen with an activation energy of only 9.3 kcal/mol (**IN22** → **TS11**). To avoid this problem, we first investigated the coupling step of terminal alkynes and secondary phosphine oxides (see the Supporting Information for details). The results showed that the P−C bond formations are quite facile (the activation barriers are 1.9 and 5.3 kcal/mol for **TS5′** and **TS6′**). More importantly, the key η^1-superoxocopper(II) intermediates **IN3** (7.2 kcal/mol; Figure 1) and **IN21** (−5.5 kcal/mol; Figure 4) may control the chemical selectivity, leading to the coupling product and oxidation product, respectively. Thus, we directly reacted (phenylethynyl)copper (0.3 mmol), NEt_3 (0.05 mmol), and $Ph_2P(O)H$ (0.25 mmol) in DMSO under air without the

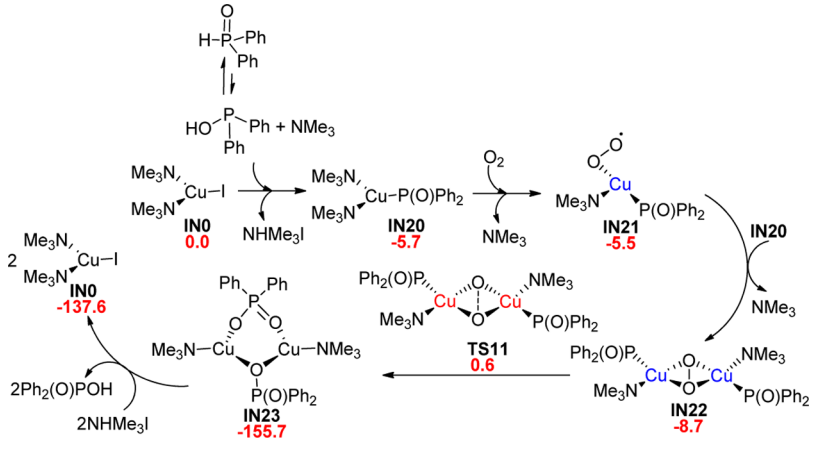


Figure 4. Free energy profile for the formation of $Ph_2P(O)OH$. Free energy values in kcal/mol are shown in red.

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presence of CuI at 55 °C for 24 h. However, the desired coupled product diphenyl(phenylethynyl)phosphine oxide was detected in only 78% NMR yield, along with a 22% yield of the oxidized product $Ph_2P(O)OH$. Presumably, the deprotonated alkyne of the alkynylcopper complex may be protonated, followed by replacement of the more nucleophilic phosphine. Thus, two strategies for preparation of diphenyl(alkynyl)-phosphine oxides were designed (Figure 5). Diphenylphosphine oxide in DMSO was added to the reaction mixture dropwise so that its concentration was minimized during the reaction course. Surprisingly, the coupled product diphenyl-(phenylethynyl)phosphine oxide (**1c**) was generated almost quantitatively, and only a trace amount of oxidized byproduct (less than 3% yield by ^{31}P NMR analysis) could be detected when the reaction was finished.

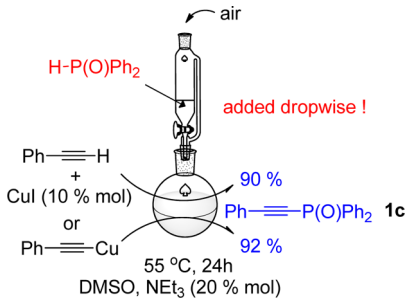

Figure 5. Two strategies for preparation of diphenyl(alkynyl)-phosphine oxides.

4. CONCLUSION

We have investigated the mechanism of Cu-catalyzed phosphorylation of terminal alkynes both experimentally and theoretically. The important role of dioxygen has been been elucidated. The dioxygen-triggered and dioxygen-free phosphorylation processes start with ligand replacement of the initial catalyst $(NMe_3)_2CuI$ to yield the alkynylcopper. In the former process, dioxygen is activated by the Cu(I) species, forming η^1-superoxocopper(II), η^2-superoxocopper(III), μ-η^2:η^2-peroxodicopper(II), and bis(μ-oxo)dicopper(III) complexes. Then proton transfer from the phosphite to the bridging oxygen atom leads to the formation of a P−C bond. In the latter process, only Cu(I) species can be located without the presence of any oxidants. The nucleophilic addition is the rate-limiting step with an activation barrier of 34.1 kcal/mol. Importantly, we found that secondary phosphine oxides are easily oxidized by dioxygen because the copper catalyst is susceptible to secondary phosphine oxides rather than dialkyl phosphonates. Further calculations confirmed this hypothesis. Therefore, diphenylphosphine oxide was added dropwise to the reaction mixture to minimize its concentration during the reaction course, leading to almost quantitative generation of the coupling product. Our findings can serve as a benchmark for other similar Cu-catalyzed dioxygen-triggered reactions, which may open a new avenue to the design of more efficient cross-coupling reactions.

5. EXPERIMENTAL SECTION

General Information. ^{31}P, ^1H, and ^{13}C NMR spectra were measured on 400 MHz spectrometers. ^1H NMR and ^{13}C NMR spectra were recorded using tetramethylsilane (TMS) as the internal standard in the solvent $CDCl_3$ (TMS at 0.00 ppm, $CHCl_3$ at 7.26 ppm for ^1H NMR; $CDCl_3$ at 77.0 ppm for ^{13}C NMR), and 85% H_3PO_4 was used as the external standard for ^{31}P NMR spectra. All coupling constant (J) values are reported in hertz.

Diethyl (Phenylethynyl)phosphonate (1a, CAS No. 3450-67-7). A mixture containing (phenylethynyl)copper (49.2 mg, 0.3 mmol), NEt_3 (60.6 mg, 0.6 mmol), $(EtO)_2P(O)H$ (34.5 mg, 0.25 mmol), and DMSO (3.0 mL) in a vial was stirred at 55 °C under air for 24 h. The solvent was evaporated under vacuum. The residue was then purified by flash chromatography (hexane/ethyl acetate = 2:1) to yield the desired diethyl (phenylethynyl)phosphonate (**1a**)[29] as an oil (54 mg, 90%).

^1H NMR ($CDCl_3$, 400 MHz): δ 7.56−7.54 (m, 2H), 7.46−7.42 (m, 1H), 7.38−7.34 (m, 2H), 4.25−4.18 (m, 4H), 1.41−1.37 (t, J = 7.1 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 132.6 (d, J_{C-P} = 2.6 Hz), 130.6, 128.5, 119.5 (d, J_{C-P} = 5.8 Hz), 99.0 (d, J_{C-P} = 53.6 Hz), 76.9 (d, J_{C-P} = 297.2 Hz), 63.2 (d, J_{C-P} = 5.5 Hz), 16.1 (d, J_{C-P} = 7.1 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ −6.4. MS (ESI) m/z: calcd for $C_{12}H_{15}O_3PNa^+$, 261.1; found, 261.1.

(*E*)-Diethyl Styrylphosphonate (1b, CAS No. 20408-33-7). A mixture containing (phenylethynyl)copper (49.2 mg, 0.3 mmol), NEt_3 (60.6 mg, 0.6 mmol), $(EtO)_2P(O)H$ (34.5 mg, 0.25 mmol), and DMSO (3.0 mL) in a vial was stirred at 55 °C under nitrogen for 24 h. The solvent was evaporated under vacuum. The residue was then purified by flash chromatography (hexane/ethyl acetate = 2:1) to yield the desired (*E*)-diethyl styrylphosphonate (**1b**)[30] as an oil (18 mg, 30%).

^1H NMR (400 MHz, $CDCl_3$): δ 7.56−7.37 (m, 6H), 6.30−6.21 (t, J = 17.5 Hz, 1H), 4.17−4.09 (m, 4H), 1.37−1.34 (t, J = 7.0 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.7 (d, J_{C-P} = 6.5 Hz), 141.0 (d, J_{C-P} = 23.3 Hz), 130.2, 128.9, 127.7, 114.5 (d, J_{C-P} = 199.2 Hz), 61.8 (d, J_{C-P} = 5.4 Hz), 16.4 (d, J_{C-P} = 6.4 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 19.6. MS (ESI) m/z: calcd for $C_{12}H_{17}O_3PNa^+$, 263.1; found, 263.1.

Diphenyl(phenylethynyl)phosphine Oxide (1c, CAS No. 7608-18-6). (i) A mixture containing CuI (7.5 mg, 0.04 mmol), NEt_3 (8.1 mg, 0.08 mmol), phenylacetylene (49.0 mg, 0.48 mmol), and DMSO (2.0 mL) in a vial was stirred at 55 °C under air for 4 h. Then diphenylphosphine oxide (81 mg, 0.4 mmol) in DMSO (2.0 mL) was added dropwise over 20 h. The solvent was evaporated under vacuum. The residue was then purified by flash chromatography (hexane/ethyl acetate = 1:1) to yield the desired diphenyl-(phenylethynyl)phosphine oxide (**1c**)[31] as a powder (109 mg, 90%). (ii) A mixture containing (phenylethynyl)copper (78.7 mg, 0.48 mmol), NEt_3 (8.1 mg, 0.08 mmol), and DMSO (2.0 mL) in a vial was stirred at 55 °C under air for 4 h. Then diphenylphosphine oxide (81 mg, 0.4 mmol) in DMSO (2.0 mL) was added dropwise over 20 h. The product was purified by the same procedure as described above to provide **1c** (111 mg, 92%).

^1H NMR ($CDCl_3$, 400 MHz): δ 7.90−7.85 (m, 4H), 7.58−7.40 (m, 9H), 7.34−7.30 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.6, 132.5 (d, J_{C-P} = 1.8 Hz), 132.3 (d, J_{C-P} = 2.8 Hz), 131.0 (d, J_{C-P} = 11.4 Hz), 130.7, 128.6, 128.6, 120.0 (d, J_{C-P} = 4.7 Hz), 105.6 (d, J_{C-P} = 30.0 Hz), 83.2 (d, J_{C-P} = 170.3 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 8.5. MS (ESI) m/z: calcd for $C_{20}H_{15}OPNa^+$, 325.1; found, 325.1.

■ ASSOCIATED CONTENT

Supporting Information

Complete refs 9a and 9b; copies of ^1H, ^{13}C, and ^{31}P NMR spectra for compounds **1a**, **1b**, and **1c**; 3D structures and Cartesian coordinates for all of the species; and free energy profiles for the oxidation step of dimethyl phosphonate and the coupling step of diphenylphosphine oxide. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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