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Homogeneous Catalysis

Efficient Oxidative Alkyne Homocoupling Catalyzed by a Monomeric Dicopper-Substituted Silicotungstate**

*Keigo Kamata, Syuhei Yamaguchi, Miyuki Kotani, Kazuya Yamaguchi, and Noritaka Mizuno**

The versatility and accessibility of polyoxometalates have led to various applications in the fields of analytical chemistry, medicine, electrochemistry, photochemistry, and catalysis,[1] particularly in the field of oxidation catalysis. Interest in catalysis by metal-substituted polyoxometalates has grown significantly because of the unique reactivity that results from the composition and structure of their active sites. To date, various kinds of metal-substituted polyoxometalates have been synthesized and applied in selective oxidation reactions.[1,2]

1,3-Diyne derivatives are very important materials in biological, polymer, and materials science because they can be converted into various structural entities, especially substituted heterocyclic compounds.[3] Oxidative alkyne–alkyne coupling is a good candidate for the synthesis of 1,3-diyne derivatives. Copper salts (stoichiometric amounts, Glaser conditions),[4] copper salts with appropriate nitrogen bases and molecular oxygen (catalytic, Hay conditions),[5] and a combination of copper and palladium salts (catalytic)[6] have commonly been used to promote oxidative alkyne–alkyne coupling.[7] However, most copper-catalyzed systems have shortcomings, especially their low turnover numbers, the formation of significant amounts of by-products, severe catalyst deactivation, narrow applicability to a limited number of alkynes, and/or the need for additives such as bases and co-catalysts.

In 1964 Bohlmann and co-workers proposed that the copper(II)-catalyzed alkyne homocoupling reaction proceeds via the formation of the alkynyldicopper(II) intermediate $\{Cu_2(\mu\text{-}C{\equiv}CR)_2\}$, which would react further to give the 1,3-diyne products directly (see the Supporting Information).[8] This reaction mechanism has generally been accepted, although some detailed mechanistic work is still necessary.[7] Thus, although it is expected that the homocoupling reaction should proceed efficiently in the presence of catalysts with a dicopper(II) core on the basis of this mechanism, an alkyne homocoupling reaction catalyzed by complexes with a dicopper(II) core is as yet unknown.[4–8]

Herein we report that the dicopper-substituted γ-Keggin silicotungstate $TBA_4[\gamma\text{-}H_2SiW_{10}O_{36}Cu_2(\mu\text{-}1,1\text{-}N_3)_2]$ (**I**, Figure 1; TBA = tetra-*n*-butylammonium)[9] is an effective homogeneous catalyst for the oxidative homocoupling of various kinds of structurally diverse alkynes [Eq. (1)]. Catalyst **I** can easily be recovered after the reaction and reused with retention of its high catalytic performance. The mechanism of the present homocoupling reaction is also investigated.

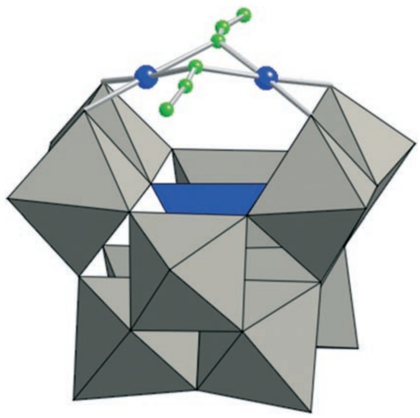

Figure 1. Polyhedral and ball-and-stick representation of the anion in $TBA_4[\gamma\text{-}H_2SiW_{10}O_{36}Cu_2(\mu\text{-}1,1\text{-}N_3)_2]$ (**I**). The $\{WO_6\}$ and $\{SiO_4\}$ units are shown as gray octahedra and a blue tetrahedron, respectively. Blue and green spheres show the copper and nitrogen atoms, respectively. Dimeric dicopper-substituted silicotungstates with azide ligands have been reported by Mialane and co-workers.[9]

$$2\,RC{\equiv}CH + 1/2\,O_2 \xrightarrow{\mathbf{I}} RC{\equiv}C{-}C{\equiv}CR + H_2O \qquad (1)$$

The oxidative homocoupling of phenylacetylene (**1a**) to give 1,4-diphenyl-1,3-butadiyne (**2a**) was carried out first under various conditions (Table 1). Among the solvents tested, benzonitrile gave **2a** in the highest yield (91%; Table 1, entry 1).[10] The reaction proceeded efficiently even under 1 atm of air, although a longer reaction time was required (Table 1, entry 2). Polar solvents such as DMSO, DMF, and acetonitrile gave **2a** in 39, 39, and 15% yields,

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[*] Dr. K. Kamata, Dr. K. Yamaguchi, Prof. Dr. N. Mizuno
Department of Applied Chemistry, School of Engineering
The University of Tokyo
7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8656 (Japan)
Fax: (+81) 358-417-220
E-mail: tmizuno@mail.ecc.u-tokyo.ac.jp

Dr. K. Kamata, Dr. S. Yamaguchi, M. Kotani, Dr. K. Yamaguchi, Prof. Dr. N. Mizuno
Core Research for Evolutional Science and Technology (CREST)
Japan Science and Technology Agency (JST)
4-1-8 Honcho, Kawaguchi, Saitama 332-0012 (Japan)

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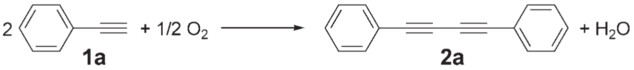
Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

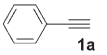
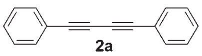
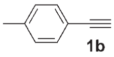
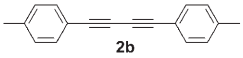
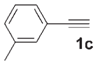
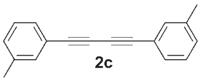
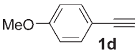
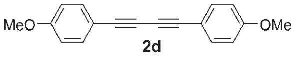
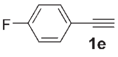
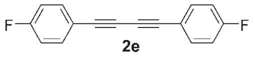
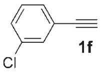
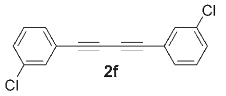
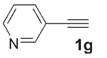
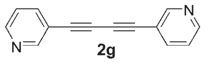
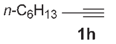
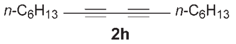
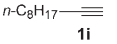
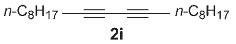
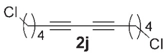
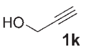
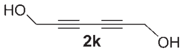
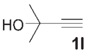
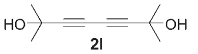
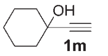
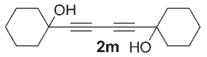
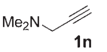
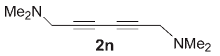
Table 1: Oxidative homocoupling of phenylacetylene (**1a**).[a]



Entry	Catalyst	Solvent	Yield of **2a**[b] [%]
1	**I**	benzonitrile	91
2[c]	**I**	benzonitrile	86
3	**I**	DMSO	39
4	**I**	DMF	39
5	**I**	acetonitrile	15
6	**I**	1,2-DCE	4
7	**I**	toluene	2
8	$TBA_4[\alpha\text{-}H_2SiW_{11}CuO_{39}]$	benzonitrile	2
9[d]	$TBA_4[\gamma\text{-}SiW_{10}O_{34}(H_2O)_2]$	benzonitrile	< 1
10[e]	$TBA_4[\gamma\text{-}SiW_{10}O_{34}(H_2O)_2] + CuCl_2$	benzonitrile	5
11	$Cu(OAc)_2$	benzonitrile	10
12	$CuCl_2$	benzonitrile	4
13	CuCl	benzonitrile	7
14	CuI	benzonitrile	2
15	Cu^I phenylacetylide	benzonitrile	< 1
16	none	benzonitrile	< 1

[a] Reaction conditions: catalyst (Cu: 4.4 mol% with respect to **1a**), **1a** (1 mmol), solvent (1 mL), 373 K, 3 h, under 1 atm of O_2. DCE = dichloroethane. [b] Determined by GC analysis using naphthalene as an internal standard. [c] The reaction was carried out under 1 atm of air for 6 h. [d] 2.2 mol%. [e] A mixture of $TBA_4[\gamma\text{-}SiW_{10}O_{34}(H_2O)_2]$ (2.2 mol%) and $CuCl_2$ (4.4 mol%) was used.

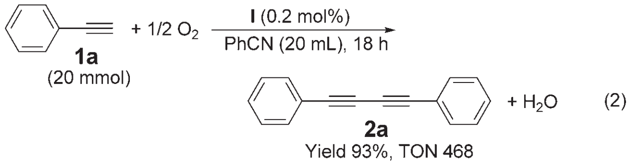
Table 2: Oxidative homocoupling of various alkynes catalyzed by **I**.[a]

Entry	Alkyne	Product	*t* [h]	Yield[b] [%]
1	 **1a**	 **2a**	3	91(88)
2[c]			3	94
3[c]			3	82
4[c]			3	88
5[c]			3	80
6	 **1b**	 **2b**	3	95(97)
7	 **1c**	 **2c**	3	97(93)
8	 **1d**	 **2d**	3	97(82)
9	 **1e**	 **2e**	3	96(89)
10	 **1f**	 **2f**	3.5	90(93)
11	 **1g**	 **2g**	2	95(82)
12	 **1h**	 **2h**	5	91(86)
13	 **1i**	 **2i**	7	92(89)
14	 **1j**	 **2j**	7	76
15	 **1k**	 **2k**	18	85
16	 **1l**	 **2l**	2	> 99(99)
17	 **1m**	 **2m**	4	90(82)
18	 **1n**	 **2n**	4	91

[a] Reaction conditions: **I** (2.2 mol% with respect to alkyne), alkyne (1 mmol), PhCN (1 mL), 373 K, 1 atm of O_2. [b] Determined by GC analysis using naphthalene as an internal standard. The values in the parentheses are the yields of isolated product. [c] These experiments used a recycled catalyst; 1 st recycle (entry 2), 2nd recycle (entry 3), 3rd recycle (entry 4), and 4th recycle (entry 5). The reaction was carried out under the same conditions as entry 1.

respectively (Table 1, entries 3–5),[11] while non-polar 1,2-dichloroethane and toluene were found to be poor solvents (Table 1, entries 6 and 7, respectively). Insoluble yellow precipitates of the copper(I) acetylide species form within a few minutes in the presence of simple Cu^I and Cu^{II} salts such as CuCl, CuI, $CuCl_2$, and $Cu(OAc)_2$ in benzonitrile under the present conditions, and the reaction proceeds very slowly (Table 1, entries 11–14). In addition, both the catalytic homocoupling of **1a** with copper(I) phenylacetylide (Table 1, entry 15) and the stoichiometric reaction with copper(I) phenylacetylide do not proceed at all, which suggests that the formation of a copper(I) acetylide species is not involved in the present catalytic cycle. The mono-copper-substituted silicotungstate $TBA_4[\alpha\text{-}H_2SiW_{11}CuO_{39}]$ (Table 1, entry 8), the non-copper-substituted silicotungstate $TBA_4[\gamma\text{-}SiW_{10}O_{34}(H_2O)_2]$[12] (Table 1, entry 9), and a mixture of $TBA_4[\gamma\text{-}SiW_{10}O_{34}(H_2O)_2]$ and $CuCl_2$ (Table 1, entry 10) were found to be almost inactive. All these results show that the dicopper $\{Cu_2(\mu\text{-}1,1\text{-}N_3)_2\}$ core in **I** plays an important role in this oxidative alkyne homocoupling.

The scope of the present catalytic oxidative homocoupling was examined with regard to a range of structurally diverse alkynes (Table 2). The selectivities for the corresponding diynes were more than 99% in all cases. The catalytic oxidative homocoupling of phenylacetylenes **1a–f**, which contain electron-donating as well as electron-withdrawing substituents, proceeded readily to afford the corresponding diyne derivatives **2a–f** in excellent yields (Table 2, entries 1–10). For example, the turnover number (TON = amount of **1a** consumed/amount of **I**) was as high as 468 in a 20-mmol-scale reaction with **1a** [Eq. (2)]. This value is the highest amongst those reported for copper-catalyzed oxidative alkyne homocoupling reactions to date (see the Supporting Information).[4–6] Furthermore, 4.5 g of **2a** (89% yield, 99% purity by ^1H NMR spectroscopy) was isolated for a 50-mmol-scale reaction. The reaction of the heteroatom-containing alkyne **1g** also proceeded efficiently (Table 2, entry 11). The aliphatic terminal alkynes **1h–1j** were also oxidized to the corresponding aliphatic diynes in high yields (Table 2, entries 12–14). Alkynes based on propargylic alcohols and amines (**1k–1n**) also gave the corresponding diynes (Table 2, entries 15–18). The catalyst can easily be recovered after the reaction by addition of an excess of diethyl ether (precipitation method), and the recovered catalyst can be recycled at least four times without significant loss of catalytic activity (Table 2, entries 2–5).



The catalytic oxidative homocoupling of **1a** shows an induction period[13] of approximately 5 min (see the Supporting Information). This induction period disappears upon pretreatment of **I** with **1a** under argon at 373 K, thereby suggesting that it is due to the reaction of **I** with an alkyne to form the catalytically active species.[14] The reactivity of **I** with **1a** was therefore investigated. Thus, 50 equivalents of **1a** with respect to **I** were added to a benzonitrile solution of **I** (4 mM) under 1 atm of argon. The resulting solution was heated to 373 K and the UV/Vis spectra of the solution were measured. A similar induction period ($\leq$ 50 min) to that observed for the above-mentioned catalytic oxidative homocoupling was observed for the formation of **2a** (see Figure 2 and the Supporting Information). During this period the intensity of the absorption band at 360 nm due to the $N_3^- \rightarrow Cu^{II}$ LMCT[15] of **I** gradually decreased and had almost disappeared after 50 min (Figure 2 a), thereby suggesting that the azido groups are eliminated from **I**.

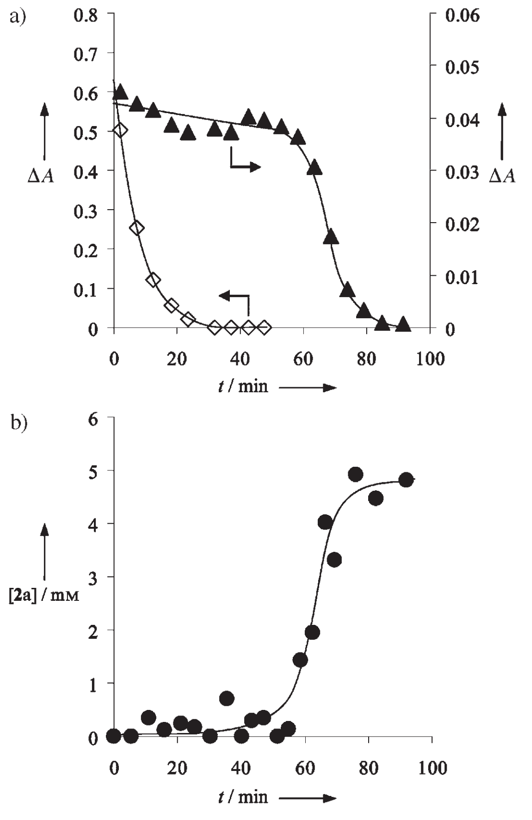


Figure 2. Time profiles of a) the absorbance at 360 (◇) and 700 nm (▲) and b) formation of **2a** from the reaction of **I** with **1a** under argon (1 atm). Reaction conditions: **I** (4 mM), **1a** (200 mM), benzonitrile (1 mL), 373 K. Changes in the UV/Vis spectra are shown in the Supporting Information. The concentration of **2a** was determined by GC analysis.

As mentioned above, the dicopper core in **I** plays an important role in the present oxidative alkyne homocoupling, and it has also been proposed that the Cu^{II}-catalyzed alkyne homocoupling reaction proceeds via formation of the alkynyldicopper intermediate $\{Cu_2(\mu\text{-}C{\equiv}CR)_2\}$.[7,8,14] It is likely that the present homocoupling proceeds via formation of a similar alkynyldicopper species formed by ligand exchange between the azido groups in **I** and alkynyl groups and that the induction period corresponds to the formation of this catalytically active alkynyl species.[16] The first-order dependence of the reaction rate on the concentration of **I** supports this proposal.

The color of the solution gradually changes from green to yellow after the induction period. An almost equimolar amount of **1a** with respect to the Cu^{II} species in **I** is converted into **2a** during the reaction, which results in a concomitant decrease in the absorption band at 700 nm due to the d–d transition of the Cu^{II} species[17] in **I** (Figure 2). This decrease suggests that all of the Cu^{II} species in **I** are reduced to Cu^{I}. Subsequent addition of molecular oxygen to the yellow solution results in a rapid color change from yellow to green and reappearance of the d-d transition of the Cu^{II} species. This change indicates that the reduced copper species in **I** is easily reoxidized by molecular oxygen. The homocoupling of **1a** proceeds at almost the same rate as that under catalytic turnover conditions after introduction of molecular oxygen (see the Supporting Information).

On the basis of all the above results, the present alkyne homocoupling reaction possibly proceeds by initial ligand exchange between the azido groups in **I** and alkynyl groups to form the alkynylcopper(II) intermediate (step 1).[7,8] This step corresponds to the induction period for the coupling reaction. The corresponding diyne is then eliminated from the alkynyl intermediate, with concomitant formation of the reduced copper species (step 2). Finally, the reduced species is reoxidized by molecular oxygen and the oxidized species reacts with an alkyne to regenerate the alkynyl intermediate (step 3). Monitoring the formation of water (benzamide)[10] during the homocoupling of **1a** with molecular oxygen revealed that the amount of water produced was the same as that of **2a**. Similarly, measurement of the molecular oxygen uptake during the homocoupling of **1a** showed that the amount of molecular oxygen consumed was half that of **2a** produced. These respective 1:1 (H_2O/diyne) and 1:2 (O_2/diyne) stoichiometries support the overall reaction shown in Equation (1). The reaction rate for the homocoupling of **1a** was found to show a first-order dependence on the concentration of **I** (7.0–28.7 mM) and to be almost independent of both the concentration of **1a** (0.7–2.0 M) and the partial pressure of molecular oxygen ($>$ 0.7 atm). No kinetic isotope effect was observed for the oxidative homocoupling of **1a** and [D1]phenylacetylene under the conditions in Table 1 (k_H/k_D = 1.0), thereby showing that C–H bond cleavage is not the rate-limiting step: the kinetic data and kinetic isotope effect show that step 2 is the rate-limiting step.

In summary, complex **I** is an effective homogeneous catalyst for oxidative alkyne homocoupling and various kinds of alkynes can be converted into the corresponding diynes in excellent yields.

Experimental Section

The dicopper-substituted γ-Keggin silicotungstate **I** was synthesized by treating $K_8[\gamma\text{-}SiW_{10}O_{36}]\cdot 12H_2O$ with $CuCl_2$ in the presence of NaN_3 (see the Supporting Information). For oxidative alkyne homocoupling reactions, catalyst **I** (2.2 mol% with respect to alkyne), the alkyne (1 mmol), and PhCN (1 mL) were placed successively in a glass reactor and the reaction mixture was stirred at 373 K under 1 atm of molecular oxygen. The yield was determined periodically by GC analysis. The diynes were isolated and purified by column chromatography on silica gel using *n*-hexane as eluent. All products were confirmed by comparing their GC retention times, and mass, ^1H, and ^{13}C NMR spectra with those of authentic samples. The purity of the isolated products was determined by ^1H NMR spectroscopy and was found to be more than 95% in each case.

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Keywords: alkynes · copper · homocoupling · homogeneous catalysis · polyoxometalates

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[11] When the oxidative coupling of **1a** in DMF was carried out in the presence of stoichiometric amounts of benzonitrile with respect to the amount of water formed, an 88% yield of **2a** was obtained after 24 h (cf. 63% yield without benzonitrile). In addition, the reaction of **1a** with 4-Å molecular sieves (200 mg, pretreated at 423 K) in DMF or DMSO gave **2a** in 90 and 86% yields, respectively, under the conditions in Table 1. These results show that benzonitrile is not a special solvent and that various other solvents can be used for this coupling reaction in the presence of water scavengers.

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[13] The length of the induction period is dependent on the concentration of **I** and **1a**. Thus, a decrease in the concentration of **I** and **1a** results in a lengthening of the induction period. An induction period of approximately 50 min is observed when the catalytic aerobic homocoupling of **1a** is carried out under the conditions in Figure 2 (see the Supporting Information).

[14] No reaction of internal alkynes such as diphenylacetylene and 2-octyne occurs in the presence of **I**, thereby suggesting that the copper species in **I** is terminally bound to an alkyne.

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