COMMUNICATIONS

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Palladium on Carbon-Catalyzed Synthesis of Benzil Derivatives from 1,2-Diarylalkynes with DMSO and Molecular Oxygen as Dual Oxidants

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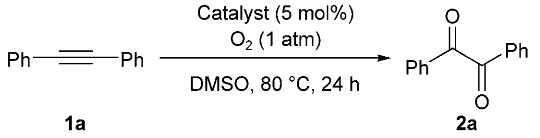
Abstract: A palladium on carbon (Pd/C)-catalyzed synthetic method for the preparation of benzil derivatives from 1,2-diarylalkynes has been established using dimethyl sulfoxide (DMSO) and molecular oxygen as dual oxidants. Regardless of the electrical nature of the functional groups on the aromatic rings, 1,2-diarylalkynes were oxidized to the corresponding benzil derivatives in high to excellent yields. Furthermore, the oxidation could efficiently be catalyzed by both the dry and wet types of Pd/C under atmospheric conditions.

Keywords: alkynes; benzil; heterogeneous catalysis; molecular oxygen; oxidation

Benzil derivatives are valuable compounds, which are found as a substructure of natural products,[1] and are utilized as corrosion inhibitors of mild steel[2] and photosensitive agents in photocurable coatings.[3] Much interest has recently focused on the benzil derivatives due to their potent activity as carboxylesterase (CE) inhibitors.[4] Moreover, a variety of biologically active heterocyclic compounds, such as imidazoles, triazines, and quinoxalines, can be synthesized from benzil derivatives.[5] Several methods have been developed for the synthesis of benzil derivatives.[6] The oxidation of 1,2-diarylalkynes, which are easily prepared by the Sonogashira coupling between arylalkynes and aryl halides,[7] is the most straightforward process. The use of a stoichiometric amount of chromium[8] or manganese oxidants,[9] ozonolysis,[1a] the sulfur trioxide-dioxane complex,[10] dioxiranes,[11,12] and iodine reagents, such as *N*-iodosuccinimide[13] or orthoperiodic acid,[14] has been essential for such reactions. These reagents or methods have several drawbacks, such as high toxicity and environmental burden, requirement of special equipments, low cost performance, and/or low yields. Dimethyl sulfoxide (DMSO), an inexpensive and widely used chemical, has been employed as an oxidant of the acid-,[15] *N*-bromosuccinimide-[16] or iodine-mediated[17] oxidation of 1,2-diarylalkynes. Although homogeneous transition metals, such as palladium(II) chloride[18] or iron(III) bromide,[19] have been reported to catalyze this transformation,[20,21] the use of a heterogeneous metal catalyst should be an attractive alternative due to its recoverability, reusability, and residual metal-free properties. Although palladium on carbon (Pd/C), a versatile heterogeneous catalyst for hydrogenation, has already been used for benzil synthesis, the method showed a narrow substrate applicability (only two examples) and required the use of homogeneous copper salts as a co-catalyst.[22] Our first attempt at the Pd/C-catalyzed oxidation of diphenylacetylene (**1a**) was performed in DMSO under an oxygen atmosphere without any other additives and afforded the corresponding benzil (**2a**) in 6% yield (Table 1, entry 1). Although rhodium, ruthenium, iridium, gold, and nickel on carbon displayed no catalyst activity (entries 2–6), platinum on carbon (Pt/C) delivered an improved yield (12% yield, entry 7).

Further investigations using Pd/C or Pt/C as the catalyst candidate were carried out to improve the reaction efficiency (Table 2). Elevation of the reaction temperature to 120 °C dramatically increased the yields of **2a** (entries 2 and 5). Using 10 mol% of 10% Pd/C, **2a** was obtained in 92% yield, while no increase

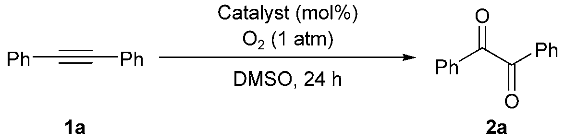
Table 1. Evaluation of activated carbon-supported transition metal catalysts.



Entry	Catalyst	Yield [%][a]
1	10% Pd/C	6
2	10% Rh/C	0
3	10% Ru/C	0
4	10% Ir/C	0
5	10% Au/C	0
6	10% Ni/C	0
7	10% Pt/C	12

[a] Isolated yield.

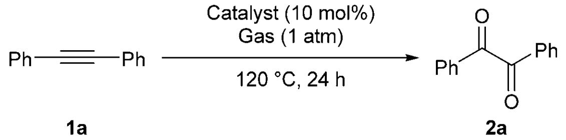
Table 2. Investigation of reaction temperature and catalyst amount.



Entry	Catalyst	Amount [mol%]	Temp. [°C]	Yield [%][a]
1	10% Pt/C	5	80	12
2		5	120	79
3		10	120	77
4	10% Pd/C	5	80	6
5		5	120	66
6		10	120	92

[a] Isolated yield.

Table 3. Determination of the role of DMSO and oxygen.[a]



Entry	Catalyst	Solvent	Gas	Ratio [%][b] **1a**:**2a**
1	10% Pd/C	DMSO	O_2	0:100
2	10% Pd/C	toluene	O_2	100:0
3	10% Pd/C	DMA	O_2	97:3
4	10% Pd/C	DMSO	Ar	71:29
5	10% Pd(II)/C	DMSO	Ar	41:59
6[c]	10% Pd(II)/C	DMSO	Ar	57:43
7[d]	10% Pd(II)/C	DMSO	Ar	0:100
8	10% Pd(0)/C	DMSO	Ar	98:2
9	10% Pd(II)/C	DMSO	O_2	0:100
10	10% Pd(0)/C	DMSO	O_2	0:100

[a] Diphenylacetylene (0.5 mmol), DMSO (0.5 mL), and catalyst (10 mol%) were used unless otherwise noted.
[b] The yield was determined by ^{1}H NMR analysis.
[c] DMSO (3 mL) was used.
[d] DMSO (3 mL) and 10% Pd(II)/C (100 mol%) were used.

in the yield was observed in the case of using 10 mol% of 10% Pt/C (entries 3 and 6). Therefore, 10% Pd/C was chosen as the optimal catalyst for this reaction.

Molecular oxygen and DMSO are two possible oxidants for the present reaction system. The oxidation hardly proceeded in toluene or *N*,*N*-dimethylacetamide (DMA) as the solvent (Table 3, entries 2 and 3) and was strongly suppressed under an argon atmosphere even in DMSO (entry 4). The yield of **2a** increased on the use of 10% Pd(II)/C instead of regular 10% Pd/C (entry 5), although the reaction hardly took place with 10% Pd(0)/C[23] (entry 8). On the other hand, the quantitative formation of **2a** was observed under an oxygen atmosphere regardless of the oxidation state of the palladium (entries 1, 9, and 10). Furthermore, the oxidation of **1a** using 1 equivalent of 10% Pd(II)/C in an increased amount of DMSO (3 mL) lead to a quantitative formation of **2a** even under an argon atmosphere (entry 7), while only an increase of DMSO in volume rather decreased the yield of **2a** (entries 5 *vs.* 6). These results suggest that DMSO is the stoichiometric oxidant and molecular oxygen serves to oxidize Pd(0) to the active Pd(II) species. A plausible pathway for the benzil synthesis is depicted in Figure 1. A Pd(II)-π-complex (**A**) is formed with alkynes, facilitating the reaction with

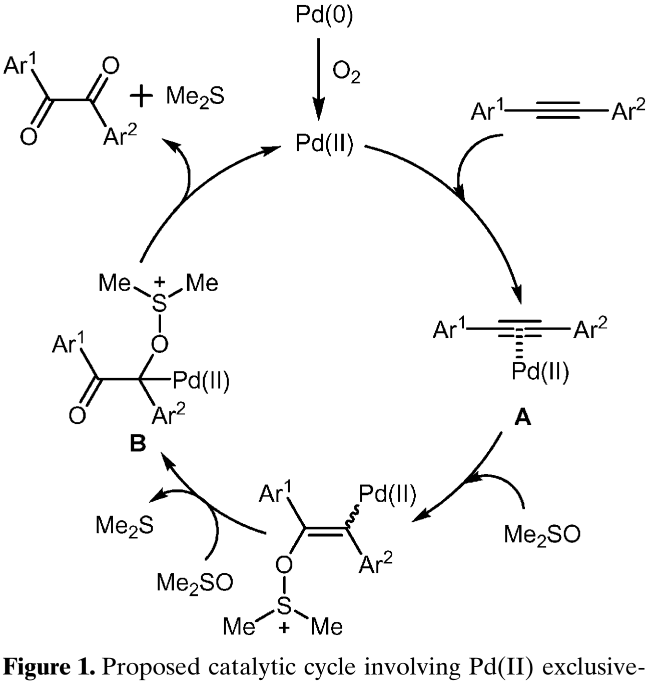


Figure 1. Proposed catalytic cycle involving Pd(II) exclusively.

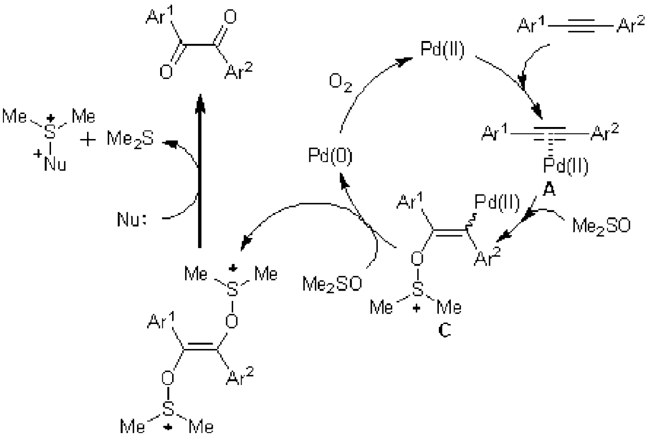
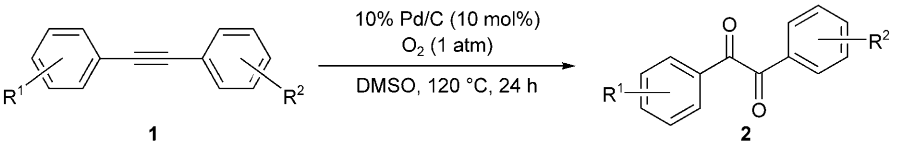


Figure 2. Proposed catalytic cycle involving a Pd(0) intermediate.

DMSO.[18,19] The nucleophilic addition of DMSO to **A** followed by the loss of dimethyl sulfide and the addition of another molecule of DMSO would afford a ketoalcohol intermediate (**B**), which would proceed to the corresponding benzil derivatives together with the palladium(II) species and a molecule of dimethyl sulfide. An alternative Wacker-type pathway, which generates palladium(0) in place of palladium(II) species *via* the formation of a vinylpalladium(II) complex (**C**), is not the prevailing reaction as is evidenced by catalytic turnover in the Pd(II) experiments in the absence of oxygen (Figure 2).

To demonstrate the scope and limitations of this method, a series of 1,2-diarylalkynes (**1a–k**) was subjected to the optimized reaction conditions (10 mol% of 10% Pd/C in DMSO at 120 °C under an oxygen at-

Table 4. Oxidation of various 1,2-diarylalkynes (**1**) to benzil derivatives (**2**) under the optimized conditions.



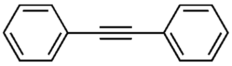
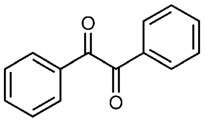
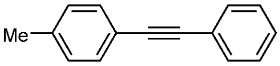
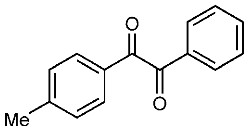
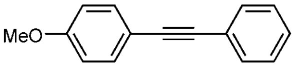
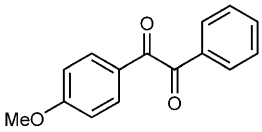
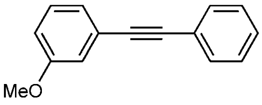
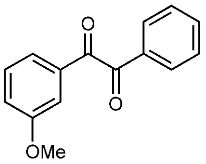
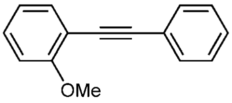
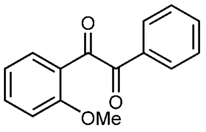
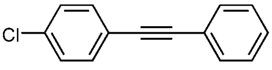
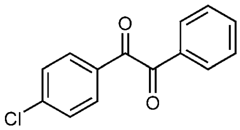
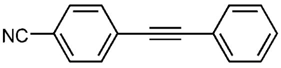
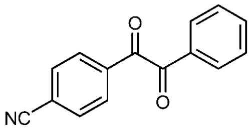
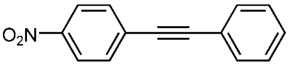
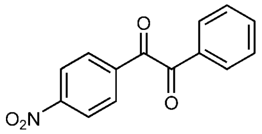
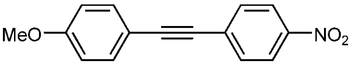
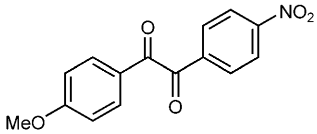
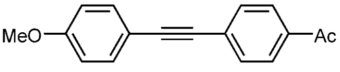
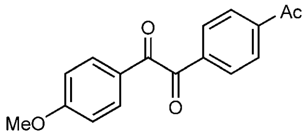
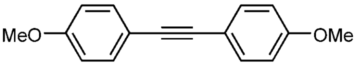
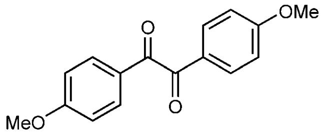
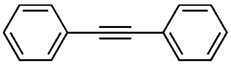
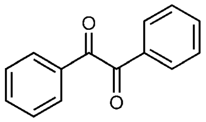
Entry	Substrate **1**		Product **2**		Yield [%][a]
1		**1a**		**2a**	92
2		**1b**		**2b**	74
3		**1c**		**2c**	85
4		**1d**		**2d**	98
5		**1e**		**2e**	61
6		**1f**		**2f**	84
7		**1g**		**2g**	49

Table 4. (Continued)

Entry	Substrate **1**		Product **2**		Yield [%][a]
8		**1h**		**2h**	41
9		**1i**		**2i**	62
10		**1j**		**2j**	74
11		**1k**		**2k**	83
12[b]		**1a**		**2a**	84

[a] Isolated yield.
[b] The reaction was performed in an air atmosphere using the wet-type 10% Pd/C (10 mol%).

mosphere, Table 4). The methyl- or methoxy-substituted 1,2-diarylalkynes (**1b–d**) were transformed into the corresponding benzil derivatives (**2b–d**) in excellent yields (entries 2–4). The oxidation of the alkyne possessing a methoxy group at the *o*-position on the aromatic ring (**1e**) afforded **2e** in a slightly lower yield, presumably due to the difficult formation of the palladium-π complex (Figure 1) by the steric hindrance around the triple bond or unexpected benzofuran formation (entry 5).[24] The introduction of an electron-withdrawing cyano or nitro group on an aromatic ring (**1g** or **1h**) suppressed the oxidation, resulting in moderate yields of the corresponding benzil derivatives (entries 7 and 8). The diphenylacetylenes bearing both electron-donating and electron-withdrawing groups on each benzene ring, **1i** and **1j**, underwent the oxidation to give **2i** and **2j** in good yields, respectively (entries 9 and 10). The smooth oxidation of the 4,4′-dimethoxydiphenylacetylene (**1k**) was also achieved (entry 11). Furthermore, it was found that the wet-type 10% Pd/C containing approximately 50% by weight of water, a preferred catalyst for industrial scale processes due to its lower ignition hazard, also efficiently catalyzed the present reaction (entry 12).

The reuse of Pd/C for the oxidation of **1a** to **2a** was next investigated. However, the yield was significantly reduced to 30% in the second run (compare with entry 1, Table 4). Therefore, fresh 10% Pd/C should be used for the present oxidation.

In conclusion, we have established a Pd/C-catalyzed environmentally benign process for the oxidation of various 1,2-diarylalkynes to the corresponding benzil derivatives using DMSO and molecular oxygen as dual oxidizing agents.[25] The present reaction efficiently proceeded without any additives and the less pyrophoric wet-type of Pd/C was also applicable. The present method is expected to provide a practical process for industry.

Experimental Section

General Procedure for the Oxidation of Diphenylacetylene (1a)

A mixture of **1a** (89.1 mg, 0.50 mmol), 10% Pd/C (53.2 mg, 0.05 mmol), and DMSO (0.5 mL), was stirred under an oxygen (balloon) atmosphere at 120 °C using the Chemistation personal organic synthesizer (EYELA, Tokyo) for 24 h. The mixture was cooled to room temperature, diluted with EtOAc (10 mL) and H_2O (10 mL), and then passed through a membrane filter (Millipore, Millex-LH, 0.45 μm). The separated organic layer was washed successively with water (2 × 10 mL) and brine (20 mL), then dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue was purified by silica gel column chromatography using *n*-hexane/EtOAc (20/1) as the eluent to give benzil (**2a**) as a colorless solid; yield: 96.7 mg (92%).

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[25] The protocol is currently limited to the synthesis of benzil derivatives. When one or two aryl groups of diarylalkynes are replaced with alkyl groups, diketone derivatives were not obtained.