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ARTICLE TYPE

A Metal-free Synthesis of Diaryl-1,2-diketones by C–C Triple Bond Cleavage of Alkynes†

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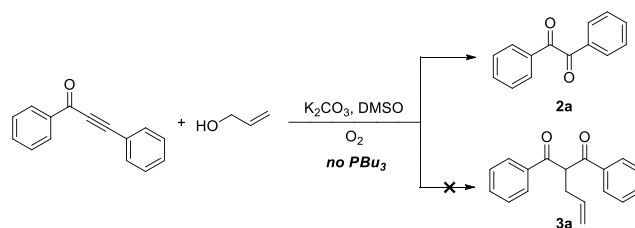
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A novel and environmentally benign protocol to diaryl-1,2-diketones has been developed. Various diaryl-1,2-diketones were afforded in moderate to excellent yields by C-C triple bond cleavage of alkynes using molecular oxygen as an oxidant. A plausible reaction mechanism was proposed that accounts for all the experimental results. The products are important building block in organic synthesis and could be converted to various synthons *via* diverse transformations.

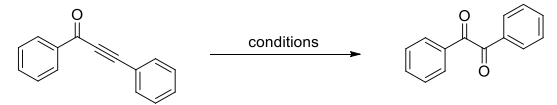
Diaryl-1,2-diketones represent an important structural moiety that appears in numerous bioactive compounds¹ and is broadly utilized for constructing various complex and highly valuable molecules.² Therefore, substantial efforts for the development of efficient synthetic strategies towards such a structure have been undertaken. The direct oxidation of internal alkynes, which could be accessible *via* Sonogashira coupling reaction, appears to be the most straightforward method to synthesize the diaryl-1,2-diketones.³ The oxidation of benzoin or hydrobenzoin in the presence of metal catalyst, such as gold,⁴ palladium,⁵ nickel,⁶ vanadium,⁷ ruthenium,⁸ thymine iron(III),⁹ molybdenum,¹⁰ and chromium trioxide¹¹ have also been reported. Recently, building diaryl-1,2-diketones from 1,3-diaryldiketones through the C-C bond cleavage has been explored as an alternative strategy.¹² However, the drawbacks associated with these procedures, such as requirement of transition metal and toxic and/or expensive starting materials, low chemo-selectivity, and harsh reaction conditions, limit their wide application in chemical industries.

During the past few years, alkynones have emerged as versatile building blocks for the construction of complicated heterocyclic rings, such as triazoles,¹³ indoles,¹⁴ quinolines,¹⁵ chromones¹⁶, furans,¹⁷ and isoxazoles.¹⁸ Recently, we have developed a tandem condensation of *o*-halo/methoxyarynylones with allylic alcohols to build 3-allyl-chromones catalyzed by PBu_3 under metal-free conditions.²⁰ However, the cleavage of C-C triple bond¹⁹ in alkyne, one of the most challenging subjects in synthetic organic chemistry, has not been reported in literature. Herein, we present a novel and environmentally friendly method for the preparation of diaryl-1,2-diketones by oxidative C-C triple bond cleavage of alkynones using molecular oxygen as an oxidant (Scheme 1).



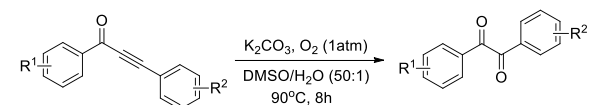
Scheme 1 Oxidative cleavage of alkynones.

The reaction of 1,3-diphenylprop-2-yn-1-one **1a** with allyl alcohol was initially conducted at 90 °C in the presence of K_2CO_3 as base in DMSO under O_2 (1 atm) atmosphere. The expected product **3a** was not observed, but diphenyl-1,2-diketone **2a** was obtained in 63% yield (Scheme 1 and Table 1, entry 1). Further studies focused on screening of the additives (entries 2–6). 1-Butanol, benzyl alcohol, and H_2O gave similar results. H_2O was chosen as additives because of its advantages in terms of economy and environment (entry 6). Increasing or decreasing the ratio of $\text{H}_2\text{O}/\text{DMSO}$ resulted in decreasing the yield of benzil **2a** (entries 7–10). The bases were also screened (entries 11–22). Cs_2CO_3 , Na_2CO_3 , and K_3PO_4 provided 63%, 48%, and 50% yields, respectively (entries 11–13). While weaker bases showed low efficiency (entries 14, 15) and stronger bases did not exhibit reactivity (entries 16–22). The solvent also played a crucial role in this transformation (entries 6 and 23–30). DMSO, DMF, and NMP afforded the desired product **2a** in 65%, 55%, and 48% yields, respectively. Only a trace amount of **2a** was observed for other solvents, such as THF, 1,4-dioxane, DCE, toluene, EtOH, and water (entries 25–30). Further optimization of the reaction parameters revealed that the combination of DMSO as solvent and O_2 as an oxidant were necessary to get successfully diaryl-1,2-diketone derivatives. On the basis of the screening reactions above, the optimal reaction conditions were identified as follows: K_2CO_3 as a base, DMSO/ H_2O (50:1) as the solvent under oxygen atmosphere at 90 °C for 8h.

Table 1 Screening various parameters for synthesis of diphenyl-1,2-diketone **2a** from 1,3-diphenylprop-2-yn-1-one^a


Entry	Additive	Solvent	Base	Yield (%) ^b
1	allyl alcohol	DMSO	K ₂ CO ₃	63
2	methanol	DMSO	K ₂ CO ₃	25
3	ethanol	DMSO	K ₂ CO ₃	30
4	1-butanol	DMSO	K ₂ CO ₃	62
5	benzyl alcohol	DMSO	K ₂ CO ₃	50
6	H₂O	DMSO	K₂CO₃	65
7	H ₂ O	DMSO	K ₂ CO ₃	55 ^c
8	H ₂ O	DMSO	K ₂ CO ₃	50 ^d
9	H ₂ O	DMSO	K ₂ CO ₃	58 ^e
10	H ₂ O	DMSO	K ₂ CO ₃	53 ^f
11	H ₂ O	DMSO	Cs ₂ CO ₃	63
12	H ₂ O	DMSO	Na ₂ CO ₃	48
13	H ₂ O	DMSO	K ₃ PO ₄	50
14	H ₂ O	DMSO	Et ₃ N	15
15	H ₂ O	DMSO	Li ₂ CO ₃	20
16	H ₂ O	DMSO	EtONa	none
17	H ₂ O	DMSO	NaH	none
18	H ₂ O	DMSO	KOtBu	none
19	H ₂ O	DMSO	NaOtBu	none
20	H ₂ O	DMSO	LiOtBu	none
21	H ₂ O	DMSO	NaOH	none
22	H ₂ O	DMSO	KOH	none
23	H ₂ O	DMF	K ₂ CO ₃	55
24	H ₂ O	NMP	K ₂ CO ₃	48
25	H ₂ O	THF	K ₂ CO ₃	trace ^g
26	H ₂ O	dioxane	K ₂ CO ₃	trace
27	H ₂ O	DCE	K ₂ CO ₃	trace
28	H ₂ O	toluene	K ₂ CO ₃	trace
29	H ₂ O	EtOH	K ₂ CO ₃	trace ^h
30	–	H ₂ O	K ₂ CO ₃	trace

^aReaction conditions: **1a** (0.5 mmol), additive/DMSO (40 μl : 2 ml), base (0.5 mmol), under O₂ atmosphere at 90 °C for 8h. ^bIsolated yield based on **1a**. ^cH₂O/DMSO (50 μl : 2 ml). ^dH₂O/DMSO (60 μl : 2 ml). ^eH₂O/DMSO (30 μl : 2 ml). ^fH₂O/DMSO (20 μl : 2 ml). ^g60 °C. ^h70 °C. DMSO = dimethylsulfoxide, NMP = 1-methylpyrrolidin-2-one.

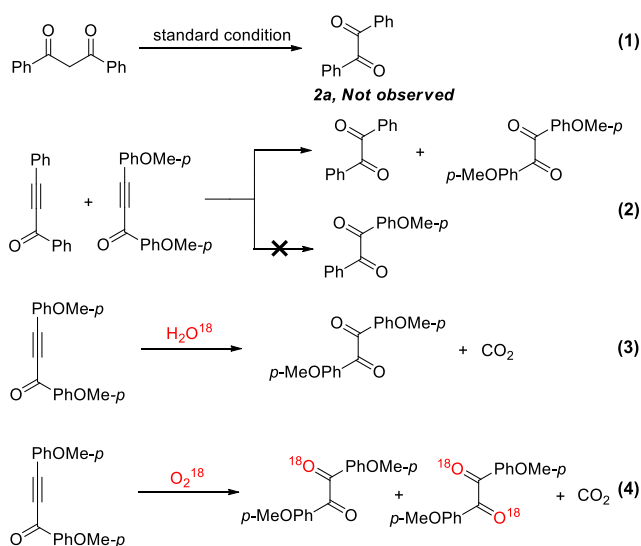
Table 2 Generality and scope of alkynes to diaryl-1,2-diketones^a


entry	Substrate	Product	Yield (%) ^b
1	1a	2a	65
2	R ¹ = OMe, R ² = H, 1b	2b	70
3	R ¹ = H, R ² = OMe, 1b'	2b	72
4	R ¹ = Me, R ² = H, 1c	2c	67
5	R ¹ = H, R ² = Me, 1c'	2c	69
6	R ¹ = <i>t</i> -Bu, R ² = H, 1d	2d	66
7	R ¹ = Cl, R ² = H, 1e	2e	38
8	R ¹ = H, R ² = Cl, 1e'	2e	45
9	R ¹ = F, R ² = H, 1f	2f	40
10	R ¹ = H, R ² = F, 1f'	2f	44
11	R ¹ = OMe, R ² = OMe, 1g	2g	93
12	R ¹ = Me, R ² = Me, 1h	2h	60
13	R ¹ = <i>t</i> -Bu, R ² = OMe, 1i	2i	65
14	R ¹ = F, R ² = OMe, 1j	2j	53
15	R ¹ = F, R ² = F, 1k	2k	40
16	R = OMe, 1l	2l	52
17	R = Me, 1m	2m	50
18	R = F, 1n	2n	35
19	1o	2o	60
20	1p	2p	51

^aReaction conditions: **1** (0.5 mmol), H₂O/DMSO (40 μl : 2 ml), K₂CO₃ (0.5 mmol), under O₂ atmosphere for 8h. ^bIsolated yield on **1**.

(entries 19, 20). The transformation of alkynes with aliphatic group was also attempted, but no desired products were observed.

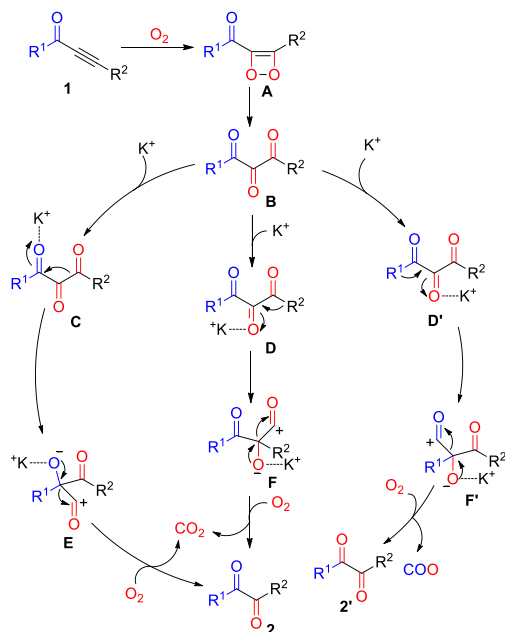
The initially proposed mechanism was suspected that 1,3-diaryldiketone might serve as an intermediate in this transformation. Unexpectedly, no desired product **2a** was detected when 1,3-diphenyldiketone was subjected under the optimal reaction conditions (Scheme 2, eq (1)). To gain more insight of the reaction mechanism, 1,3-diphenylprop-2-yn-1-one and 1,3-bis(4-methoxyphenyl)prop-2-yn-1-one were treated in one pot under the standard reaction conditions (Scheme 2, eq (2)). The potential crossover products were not detected by GC-MS, which indicated that this transformation probably occurred through an intramolecular process. In order to confirm the source of the oxygen atom of diaryl-1,2-diketone, the controlled experiments were conducted involving H₂O¹⁸ and O₂¹⁸, respectively. The results showed that the oxygen atom of the diaryl-1,2-diketone derived from O₂, but not from H₂O. Furthermore, CO₂ was generated and caused the clear limewater to become cloudy (Scheme 2, eq (3) and eq (4)).



Scheme 2 The controlled experiments for exploring the reaction mechanism.

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According to the results obtained and literatures²¹, the mechanistic pathways of this oxidative cleavage metathesis were proposed and presented in Scheme 3. The initial step of the reaction involved the formation of 1,2-dioxetene **A** from the alkynone **1** with molecular oxygen. Then thermally inducing the transformation of intermediate **A** gave 1,2,3-tricarbonyl compound **B**. Subsequently, activation of the β -keto or α -keto moiety of compound **B** in the presence of K_2CO_3 led to intermediates **C**, **D**, and **D'**, followed by C-C bond cleavage and the carbon immigration to intermediates **E**, **F** and **F'**, respectively. Finally, the elimination of carbon monoxide (CO) from intermediate **E**, **F** and **F'** provided the desired diaryl-1,2-diketone **2** and **2'**. Simultaneously, the gas carbon dioxide (CO_2) was formed by the oxidation of CO with molecular oxygen.



Scheme 3 Plausible reaction mechanism.

In conclusion, we have developed a novel and environmentally benign method for the synthesis of diaryl-1,2-diketones with high chemo-selectivity by C-C triple bond cleavage of alkynones. The oxidation of triple bond, cleavage of C-C bond and carbon immigration were involved in this procedure.

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