JOC The Journal of Organic Chemistry
Article
Cite This: J. Org. Chem. XXXX, XXX, XXX−XXX
pubs.acs.org/joc

ICl/$AgNO_3$ Co-Catalyzed Radical Oxidation of Diaryl- and Alkylarylalkynes into 1,2-Diketones

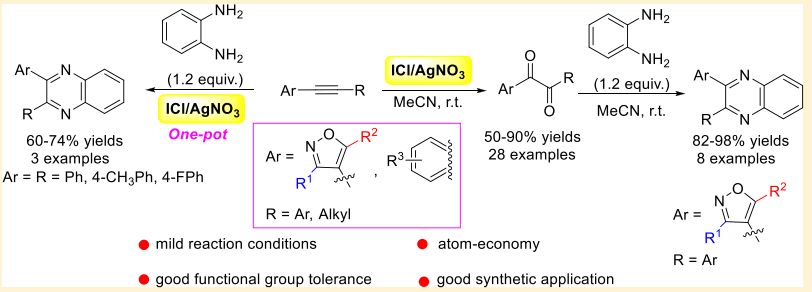
Wen Yang,[†] Yu Chen,[‡,§] Yongqi Yao,[†] Xin Yang,[†] Qifu Lin,[†] and Dingqiao Yang*[,†]

[†]Key Laboratory of Theoretical Chemistry of Environment, Ministry of Education, School of Chemistry and Environment, South China Normal University, Guangzhou 510006, People's Republic of China

[‡]Department of Chemistry and Biochemistry, Queens College of the City University of New York, 65-30 Kissena Blvd., Queens, New York 11367, United States

[§]Ph.D. Program in Chemistry, The Graduate Center of the City University of New York, 365 Fifth Avenue, New York, New York 10016, United States

Supporting Information



ABSTRACT: A novel ICl/$AgNO_3$ co-catalyzed radical oxidation of diaryl- and alkylarylalkynes into 1,2-diketones is reported. The reaction proceeded smoothly under mild conditions and generated 1,2-diketones in moderate to good yields with a good tolerance of functional groups. Furthermore, the obtained C4-(1,2-diketoaryl)isoxazoles could react smoothly with 1,2-diaminobenzene to form C4-(3-arylquinoxalin-2-yl)isoxazoles. At last, a new one-pot strategy for the synthesis of quinoxalines from 1,2-diphenylethynes and 1,2-diaminobenzene is also reported.

INTRODUCTION

1,2-Dicarbonyl derivatives are one of the most important structural motifs, since they are not only found in many natural products and bioactive molecules[1] but also broadly serve as useful building blocks in the construction of medicinally relevant heterocycles,[2] such as imidazoles, pyrazines, and quinoxalines. They are also used in materials chemistry[3] and as ligands for various metal complexes.[4] Therefore, numerous methods have been developed for their synthesis. For example, transition-metal- or metal-free-catalyzed oxidative synthesis of 1,2-diketones,[5] photo-catalyzed synthesis of 1,2-diketones.[6]

Over the past few years, metal nitrates have been applied to the oxidative reaction of diarylalkynes, as shown in Scheme 1. In 1972, Taylor and co-workers reported $Ti(NO_3)_3$-catalyzed oxidative synthesis of 1,2-diketones (Scheme 1a).[7] Recently, Jung and Deng developed a method for the oxidation of internal alkynes to 1,2-diketones in the presence of $Hg(NO_3)_2$−H_2O (Scheme 1b).[8] Subsequently, König and Wille described $LiNO_3$-mediated and visible light photoredox-catalyzed oxidation of phenylacetylene to benzil (Scheme 1c).[9] In 2019, Thongsornkleeb and co-workers reported $Ce(NH_4)_4(NO_3)_6$-promoted $Pd(PPh_3)_2Cl_2$-catalyzed oxidative synthesis of 1,2-diketones (Scheme 1d).[10] Although the methods of metal nitrate-catalyzed oxidative synthesis of 1,2-diketones have been reported, there are still several drawbacks: (a) the use of high toxic $Ti(NO_3)_3$ and harsh reaction conditions; (b) the use of high toxic $Hg(NO_3)_2$; (c) low yield of benzil; and (d) the use of a bimetallic reagent system ($Pd(PPh_3)_2Cl_2$/$Ce(NH_4)_4(NO_3)_6$) and high temperature. Therefore, developing a mild and efficient method for the catalytic oxidation of internal alkynes is still highly desirable. Recently, the reactions of iodide-mediated oxidative synthesis of 1,2-diketones have also been reported.[11] The reported methods showed that the iodide could promote the process of oxidative synthesis of 1,2-diketones. Therefore, we try to combine iodide and metal nitrate to co-catalyze the oxidative synthesis of 1,2-diketones from diarylalkynes, aiming to overcome the drawbacks of metal nitrates.

Recently, our group successfully synthesized a series of C4-alkynylisoxazles.[12] Therefore, we chose the C4-alkynylisoxazles as substrates to test the feasibility of our ideas.

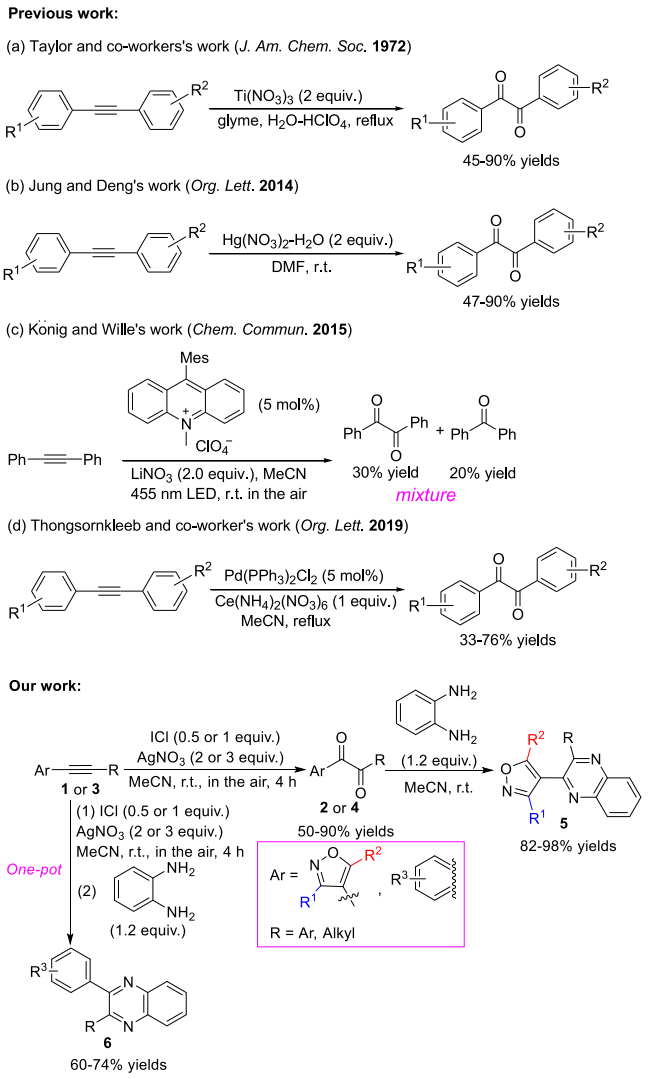
RESULTS AND DISCUSSION

In our initial study, 3,5-diphenyl-4-(*p*-tolylethynyl)isoxazole (**1a**) was chosen as the model substrate to optimize the

Received: June 21, 2019

DOI: 10.1021/acs.joc.9b01667
J. Org. Chem. XXXX, XXX, XXX−XXX

Scheme 1. Previous Work and Our Work



reaction conditions. To our delight, the model reaction proceeded smoothly and generated 1-(3,5-diphenyl-isoxazol-4-yl)-2-*p*-tolylethane-1,2-dione (**2a**) in 69% yield in the presence of ICl (1 equiv) and $AgNO_3$ (3 equiv) as co-catalysts in MeCN under an air atmosphere for 4 h at room temperature (Table 1, entry 1). The structure of **2a** was confirmed by single-crystal X-ray crystallography.[13] It should be noted that in the absence of ICl or $AgNO_3$, none of the targeted product was observed even when the reaction time was 12 h and the starting material was recovered (Table 1, entries 2−3). Subsequently, various metal nitrates, including KNO_3, $LiNO_3$, and $Ce(NH_4)_2(NO_3)_6$ were tested in the reaction. All of them afforded the targeted product **2a** with low yields (Table 1, entries 4−6). When $AgNO_2$ was applied, the reaction could not proceed at all (Table 1, entry 7). Other silver salts, such as AgOAc, AgOTf, Ag_2O, and Ag_2CO_3, only afforded a trace of the targeted product **2a** (Table 1, entries 8−11). The effect of the solvents on the reaction was also investigated, and MeCN turned out to be the best choice among the tested solvents including dimethylformamide (DMF), 1,2-dichloroethane (DCE) and tetrahydrofuran (THF) (Table 1, entries 1 vs 12−14). The loading of ICl and $AgNO_3$ in the reaction was also optimized (Table 1, entries 15−18). The results showed that 1 equiv of ICl and 2 equiv of $AgNO_3$ were the best, affording the targeted product **2a** in 82% yield (Table 1, entry 15). Another two iodine sources, such as I_2 and NIS (*N*-iodosuccinimide), were also tested and provided the targeted product **2a** in moderate yields (69 and 59%, respectively).

With the optimized reaction conditions in hand (Table 1, entry 15), the scope of ICl/$AgNO_3$ co-catalyzed oxidation of 3,5-disubstituted-4-alkynylisoxazoles into 3,5-disubstituted-4-(1,2-diketoaryl)isoxazoles was investigated, as shown in Table 2. First, we examined the effect of varying R^1 group on the yield, while retaining R^2 as a phenyl group and R^3 as a 4-CH_3 group. The reaction occurred smoothly when R^1 was a *tert*-butyl and isopropyl group, affording the corresponding products **2b** and **2c** in good yields (73 and 70%, respectively). Subsequently, R^2 groups on the effect of the reaction were also investigated, while retaining R^1 as a phenyl group and R^3 as a 4-CH_3 group. The results indicated that the R^2 group (*tert*-butyl, cyclopropyl, and *n*-pentyl) had no distinct effect on the reaction, affording the corresponding products **2d**−**2e** in good yields (78, 71, and 75%, respectively). In addition, the substrates (**1g**−**1i**) bearing an electron-donating group on the C3 position of isoxazole had a better compatibility than the electron-withdrawing group, and afforded the corresponding targeted products **2g**−**2i** in good yields (76, 65, and 70%, respectively). At last, we investigated the effect of the R^3 group on the reaction, while retaining R^1 = R^2 = Ph. All of the targeted products **2j**, **2l**−**2n** could be obtained in good yields (75, 79, 78, and 60%, respectively) except **2k** (50% yield).

The scope of this oxidative reaction was further expanded to diaryl-, alkylaryl- and dialkylalkynes, as shown in Table 3. The benzil **4a** could only be obtained in 62% yield under our optimized reaction conditions (Table 1, entry 15). To our delight, the yield of **4a** could be increased to 90% in the presence of 0.5 equiv of ICl and 3 equiv of $AgNO_3$ in MeCN for 4 h under an air atmosphere at room temperature. Subsequently, a variety of 1,2-diarylacetylenes were subjected to the reaction. In general, symmetrical and unsymmetrical diarylacetylenes with different substituents on the aromatic units were found to be feasible for the reaction and could afford the corresponding targeted products (**4a**−**4l**) in good to excellent yields (60−90%) with a good functional group tolerance. In addition, the results showed that substrates bearing an electron-donating group (CH_3) or an electron-withdrawing group (F, Cl, Br, CF_3, NO_2, $COCH_3$, and CN) afforded the desired products in excellent yields. However, substrate **3b** bearing the OCH_3 group only produced targeted product **4b** in 60% yield. In order to further extend the scope of the reaction, 2-(phenylethynyl)thiophene **3m** and but-1-yn-1-ylbenzene **3n** were used as the substrates, which afforded the corresponding products (**4m** and **4n**) in good yields (87 and 75%, respectively). However, when 3-hexyne **3o** and 2-butyne **3p** were applied to the reaction, no corresponding product 1,2-diketones (**4o** and **4p**) were observed.

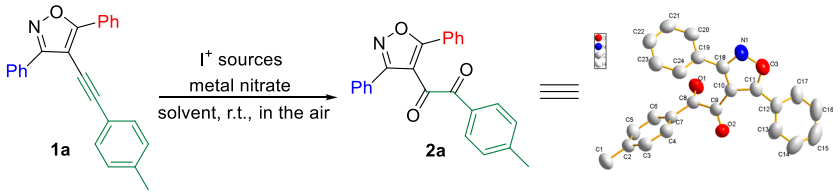
To further demonstrate the synthetic application of C4-(1,2-diketoaryl)isoxazoles, C4-(3-arylquinoxalin-2-yl)isoxazoles **5a**−**5h** could be easily obtained in 82−98% yields from C4-(1,2-diketoaryl)isoxazoles and 1,2-diaminobenzene in MeCN at room temperature (Scheme 2a).

With the high efficiency and mild conditions of the oxidation reaction in our hand (conditions: 0.5 equiv of ICl, 3 equiv of $AgNO_3$, and MeCN, rt, in air), quinoxalines **6a**−**6c** could be obtained in 60−74% yields via a one-pot strategy (Scheme 2b).

To illustrate a plausible mechanism for the oxidative reaction, several control experiments were conducted and the

DOI: 10.1021/acs.joc.9b01667
J. Org. Chem. XXXX, XXX, XXX−XXX

Table 1. Optimization of Reaction Conditions[a]



entry	catalyst (equiv)	metal nitrate (equiv)	solvent	time (h)	yield (%)[b]
1	ICl (1)	$AgNO_3$ (3)	MeCN	4	69
2	ICl (1)		MeCN	12	n. r.
3		$AgNO_3$ (3)	MeCN	12	n. r.
4	ICl (1)	KNO_3 (3)	MeCN	12	5
5	ICl (1)	$LiNO_3$ (3)	MeCN	12	7
6	ICl (1)	$Ce(NH_4)_2(NO_3)_6$ (3)	MeCN	12	20
7	ICl (1)	$AgNO_2$ (3)	MeCN	12	n. r.
8	ICl (1)	AgOAc (3)	MeCN	12	trace
9	ICl (1)	AgOTf (3)	MeCN	12	trace
10	ICl (1)	Ag_2O (3)	MeCN	12	trace
11	ICl (1)	Ag_2CO_3 (3)	MeCN	12	trace
12	ICl (1)	$AgNO_3$ (3)	DMF	12	20
13	ICl (1)	$AgNO_3$ (3)	DCE	12	trace
14	ICl (1)	$AgNO_3$ (3)	THF	12	7
15	**ICl (1)**	**$AgNO_3$ (2)**	**MeCN**	**4**	**82**
16	ICl (1)	$AgNO_3$ (1)	MeCN	12	69
17	ICl (0.5)	$AgNO_3$ (2)	MeCN	12	56
18	ICl (0.1)	$AgNO_3$ (2)	MeCN	12	10
19	I_2 (1)	$AgNO_3$ (2)	MeCN	4	69
20	NIS (1)	$AgNO_3$ (2)	MeCN	4	59

[a]Reaction conditions: **1a** (0.125 mmol, 1.0 equiv), catalyst (0.5−1 equiv), metal nitrate (1−3 equiv), and solvent (2.5 mL), under an air atmosphere at room temperature. [b]Isolated yields.

results are summarized in Scheme 3. When 2,2,6,6-tetramethyl-1-piperidinyloxyl and 2,6-di-*tert*-butyl-4-methylphenol, two commonly used radical scavengers, were added to the reaction, respectively, no desired product **2a** was obtained in either case, suggesting that this transformation might occur via a radical mechanism (Scheme 3a). The oxidation of **1a** under a N_2 atmosphere proceeded in essentially the same manner, which afforded **2a** in 79% yield (Scheme 3b). Meanwhile, when the model reaction proceeded in $H_2{}^{18}O$, a mono ^{18}O labeled product was observed with a ratio of **2a**/**2a**-mono ^{18}O/**2a**-di ^{18}O in 74:25:1 (Scheme 3c). It should be noted that the 1,2-diketones are very active, and the oxygen of the carbonyl group can be exchanged with the oxygen of water.[5f,j,14] Therefore, it is obvious that the sole source of the two oxygen atoms of **2a** is from $AgNO_3$.

Based on the above results described and related in the literature,[9,11e,15] a plausible mechanism for this radical oxidative reaction was proposed, as shown in Scheme 4. First, ICl reacted with $AgNO_3$ to produce a AgCl precipitation and $IONO_2$ **A**, and then $IONO_2$ **A** may undergo homolytic cleavage to yield a nitrate radical under this reaction condition. Addition of the nitrate radical to **1a** generated intermediate **B**. Subsequently, intermediate **B** reacted with $IONO_2$ **A**, iodine radical or ICl to afford intermediate **C**. Intermediate **C** was then attacked by the nitrate radical or $IONO_2$ **A**, affording intermediate **D** and a nitrogen dioxide radical, and then a nitrogen dioxide radical left as a leaving group. Finally, the intermediate **D** was attacked by another nitrate radical to produce the desired product **2a**, as well as a nitrogen dioxide radical and $IONO_2$ **A**. Further investigations on the more detailed reaction mechanism are ongoing in our laboratory.

CONCLUSIONS

In summary, we have developed a mild and efficient method for the synthesis of 1,2-diketones by ICl/$AgNO_3$ co-catalyzed radical oxidation of diaryl- and alkylarylalkynes. The reaction is likely to go through a radical oxidation mechanism and a detailed mechanistic study is underway in our laboratory. The obtained C4-(1,2-diketoaryl)isoxazoles could be easily converted into corresponding C4-(3-arylquinoxalin-2-yl)-isoxazoles. Under the reaction conditions, quinoxalines could be synthesized by a one-pot strategy. As the newly synthesized C4-(1,2-diketoaryl)isoxazoles and C4-(3-arylquinoxalin-2-yl)-isoxazoles are biologically important compounds, future studies will be focused on evaluating the biological and pharmaceutical activities of these compounds.

EXPERIMENTAL SECTION

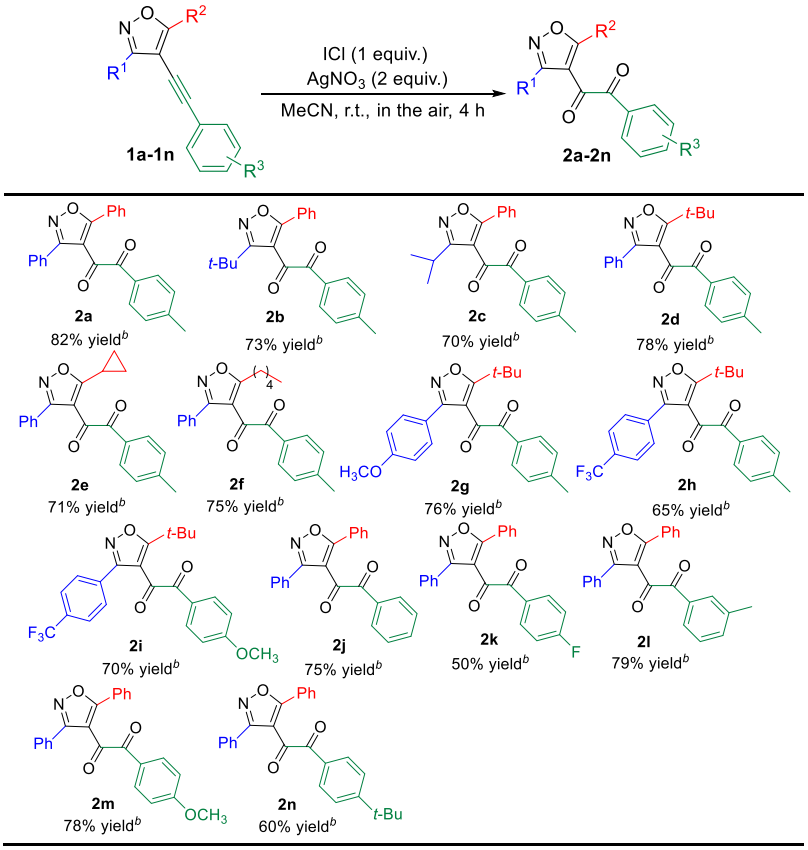
General Information. All reactions were carried out in 10/100 mL round-bottomed flask unless otherwise indicated. Analytical thin layer chromatography (TLC) was performed with SiliCycle normal phase glass plates (0.25 mm, 60 Å pore size, 230−400 mesh). Visualization was done under a 254 nm UV light source.

Materials. Unless otherwise indicated, all reagents and solvents were purchased from commercial suppliers and used without additional purification. Compounds **1a−1h** and **1j−1n** were prepared using our previously published methods.[12] Compounds **3a** and **3n−3p** were commercially available and were used directly in the reaction.

Instrumentation. All ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded at 600/400 MHz and 150/100 MHz, respectively, using

DOI: 10.1021/acs.joc.9b01667
J. Org. Chem. XXXX, XXX, XXX−XXX

Table 2. Scope of Substrates 1a−1n[a]



[a]Reaction conditions: **1** (0.125 mmol, 1.0 equiv), ICl (1.0 equiv), $AgNO_3$ (2.0 equiv), and MeCN (2.5 mL), under an air atmosphere at room temperature. [b]Isolated yield.

$CDCl_3$ as the solvent. ^{19}F NMR spectra were recorded at 564 MHz at 25 °C in $CDCl_3$. Spectral data are reported as follows: chemical shift (δ, ppm); multiplicity (s-singlet, d-doublet, t-triplet, q-quadruplet, and m-multiplet); coupling constants (J, Hz) and number of protons. The chemical shifts of all ^1H and $^{13}C\{^1H\}$ NMR spectra are referenced to the residual signal of $CDCl_3$ (δ 7.26 ppm for the ^1H NMR spectra and δ 77.23 ppm for the $^{13}C\{^1H\}$ NMR spectra). HRMS (ion trap) were obtained from mass spectrometry (ESI). Melting points were recorded on an electrothermal digital melting point apparatus and were uncorrected.

Procedure for the TLC Silica Gel Preparative Plate. In a 1.5 L beaker, carboxymethylcellulose sodium (CMC, 8 g) and 1 L deionized water were added. After CMC was completely dissolved in deionized water, GF254 silica gel was added (350 g) and kept for overnight stirring. The obtained thick slurry was spread on a glass plate (20 cm × 20 cm). The resultant glass plate was dried and activated by heating in an oven for 10 min at 100 °C.

Synthesis of Substrate 1i. Substrate 5-(*tert*-butyl)-4-((4-methoxyphenyl)ethynyl)-3-(4-(trifluoromethyl)phenyl)isoxazole **1i** was synthesized according to the literature.[12] A 10 mL two-neck round-bottomed flask with a reflux condenser was flame-dried under a stream of nitrogen and cooled to room temperature. 5-(*tert*-butyl)-4-iodo-3-(4-(trifluoromethyl)phenyl)isoxazole (118.5 mg, 0.3 mmol, 1.0 equiv), $Pd(acac)_2$ (4.7 mg, 5 mol %), PPh_3 (7.9 mg, 10 mol %), CuI (5.8 mg, 10 mol %), and Et_2NH (43.9 mg, 2 equiv) were added, followed by the addition of anhydrous DMF (2.5 mL). The flask was flushed with nitrogen and the 1-ethynyl-4-methoxybenzene (1.0 M in DMF, 2.0 equiv) was added gradually by using a syringe. The resulting solution was allowed to stir at 60 °C in an oil bath until completion, as monitored by TLC. After cooling to room temperature, the reaction was poured into 10 mL ethyl acetate and washed three times (3 × 10 mL) with water. The organic layers were combined, dried with anhydrous $MgSO_4$, and then filtered. The filtrate was concentrated under vacuum, and the resulting residue was purified by column chromatography on silica gel (200−300 mesh) using ethyl acetate/petroleum ether as eluent to afford the desired product **1i**.

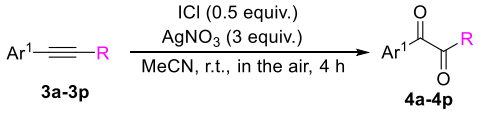
*5-(tert-Butyl)-4-((4-methoxyphenyl)ethynyl)-3-(4-(trifluoromethyl)phenyl)isoxazole (**1i**).* Substrate **1i** was obtained as a colorless oil (105.4 mg, 88% yield). R_f = 0.26 on silica gel (ethyl acetate/petroleum ether 1:50, v/v). ^1H NMR (600 MHz, $CDCl_3$): δ 8.21 (d, J = 8.2 Hz, 2H), 7.74 (d, J = 8.2 Hz, 2H), 7.41 (d, J = 8.8 Hz, 2H), 6.93−6.87 (m, 2H), 3.84 (s, 3H), 1.57 (s, 9H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 182.4, 161.1, 160.2, 132.8, 132.6, 131.9 (q, J = 31.5 Hz), 128.3, 125.7 (q, J = 4.5 Hz), 124.4 (q, J = 270.0 Hz), 114.9, 114.4, 97.2, 96.4, 77.6, 55.5, 34.9, 28.5. ^{19}F NMR (564 MHz, $CDCl_3$): δ −62.79. HRMS (ESI-ion trap) m/z: $[M + H]^+$ calcd for $C_{23}H_{21}F_3NO_2$, 400.1524; found, 400.1515.

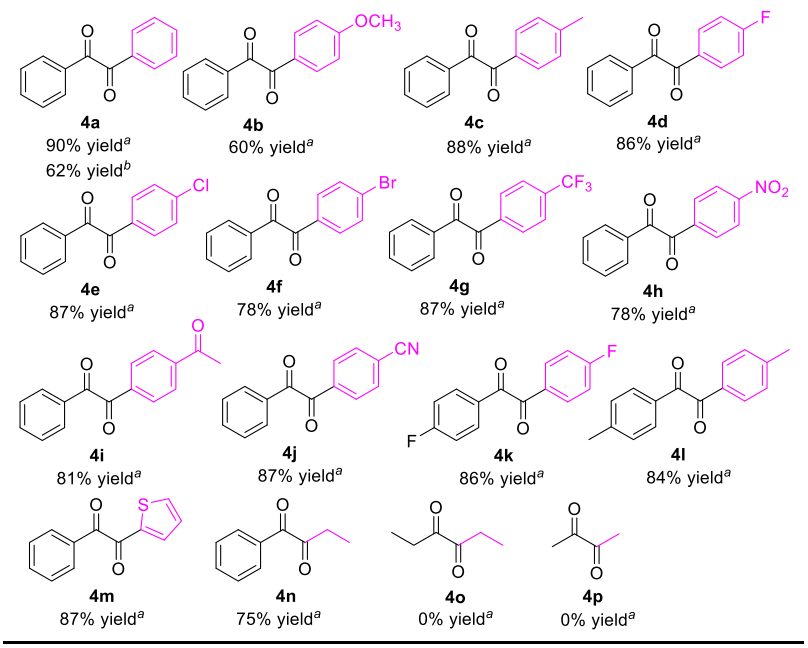
General Procedure (I) for the Synthesis of Alkynes (3). To a 100 mL round-bottomed flask CuI (14.3 mg, 1.5 mol %), $Pd(PPh_3)_2Cl_2$ (70.2 mg, 2% mmol), triethylamine (15 mL), and THF (10 mL) were added. The flask was flushed with nitrogen, and aryl iodine (5.0 mmol, 1 equiv) was added to the stirred suspension, followed by immediate dropwise addition of terminal alkyne (4.5 mmol). The resulting mixture was allowed to stir at room temperature overnight. Water (10 mL) was added to the reaction mixture. The resulting mixture was extracted with ethyl acetate (3 × 20 mL). The organic layers were combined and dried over anhydrous $MgSO_4$. The solvent was removed under vacuum, and the residue was purified by column chromatography on silica gel (200−300 mesh) using ethyl acetate/petroleum ether as the eluent to afford the desired products **3**.

*1-Methoxy-4-(phenylethynyl)benzene (**3b**).* Following general procedure (**I**), substrate **3b** was obtained as a yellow solid (0.66 g, 70% yield), mp 93−95 °C. R_f = 0.25 on silica gel (ethyl acetate/

DOI: 10.1021/acs.joc.9b01667
J. Org. Chem. XXXX, XXX, XXX−XXX

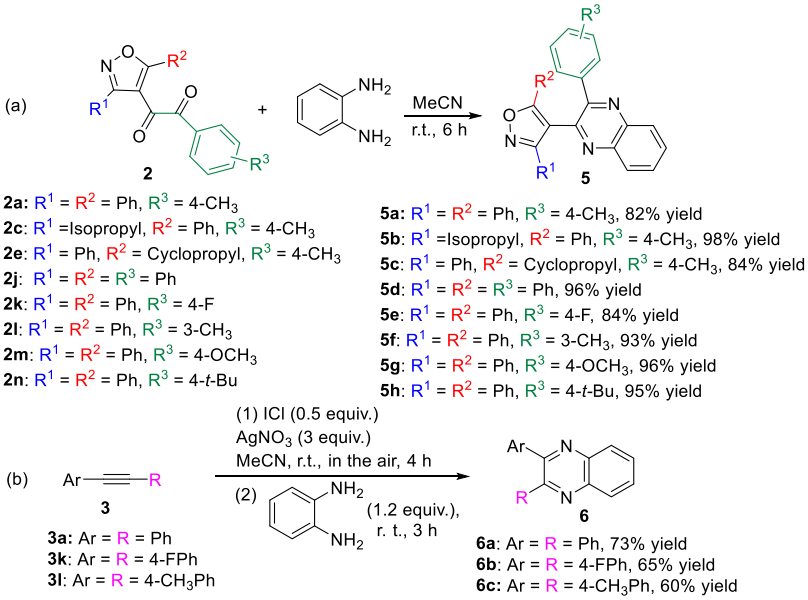
Table 3. Scope of Oxidation of Alkynes into 1,2-Diketones[a]





[a]Reaction conditions: **3** (0.15 mmol, 1.0 equiv), ICl (0.5 equiv), $AgNO_3$ (3.0 equiv), and MeCN (2.5 mL), under an air atmosphere at room temperature. [b]ICl (1 equiv), $AgNO_3$ (2 equiv).

Scheme 2. Synthesis of C4-(3-Arylquinoxalin-2-yl)isoxazoles 5a−5h and Quinoxalines 6a−6c



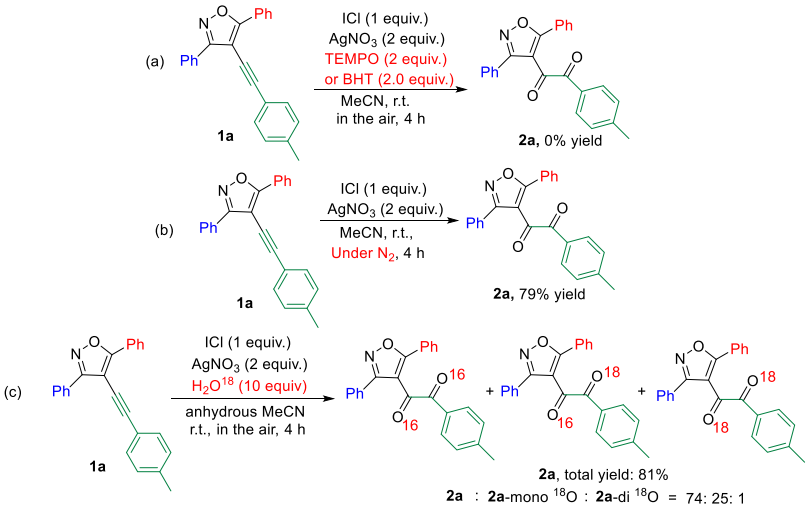
petroleum ether 1:30, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.53−7.47 (m, 4H), 7.37−7.30 (m, 3H), 6.91−6.87 (m, 2H), 3.83 (s, 3H). The ^{1}H NMR spectral data are in good agreement with the literature data.[16]

*1-Methyl-4-(phenylethynyl)benzene (**3c**).* Following general procedure (**I**), substrate **3c** was obtained as a white solid (0.70 g, 80% yield), mp 70−72 °C. R_f = 0.91 on silica gel (petroleum ether). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.55−7.53 (m, 2H), 7.45 (d, J = 8.1 Hz, 2H), 7.36−7.34 (m, 3H), 7.17 (d, J = 7.9 Hz, 2H), 2.38 (s, 3H). The ^{1}H NMR spectral data are in good agreement with the literature data.[17]

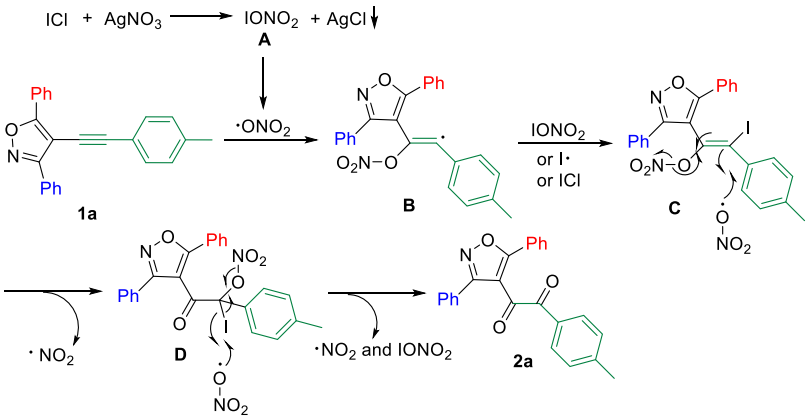
*1-Fluoro-4-(phenylethynyl)benzene (**3d**).* Following general procedure (**I**), substrate **3d** was obtained as a white solid (0.62 g, 70% yield), mp 108−110 °C. R_f = 0.92 on silica gel (petroleum ether). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.53−7.49 (m, 4H), 7.39−7.32 (m, 3H), 7.11−7.02 (m, 2H). The ^{1}H NMR spectral data are in good agreement with the literature data.[17]

DOI: 10.1021/acs.joc.9b01667
J. Org. Chem. XXXX, XXX, XXX−XXX

Scheme 3. Control Experiments



Scheme 4. Plausible Mechanism



*1-Chloro-4-(phenylethynyl)benzene (**3e**).* Following general procedure (**I**), substrate **3e** was obtained as a white solid (0.82 g, 85% yield), mp 81−83 °C. R_f = 0.89 on silica gel (petroleum ether). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.54−7.51 (m, 2H), 7.50−7.47 (m, 2H), 7.40−7.35 (m, 5H). The ^{1}H NMR spectral data are in good agreement with the literature data.[18]

*1-Bromo-4-(phenylethynyl)benzene (**3f**).* Following general procedure (**I**), substrate **3f** was obtained as a white solid (0.93 g, 80% yield), mp 83−85 °C. R_f = 0.91 on silica gel (petroleum ether). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.53−7.55 (m, 2H), 7.49−7.45 (m, 2H), 7.39−7.31 (m, 5H). The ^{1}H NMR spectral data are in good agreement with the literature data.[19]

*1-(Phenylethynyl)-4-(trifluoromethyl)benzene (**3g**).* Following general procedure (**I**), substrate **3g** was obtained as a white solid (0.98 g, 88% yield), mp 103−105 °C. R_f = 0.95 on silica gel (petroleum ether). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.63 (q, J = 8.4 Hz, 4H), 7.59−7.53 (m, 2H), 7.41−7.35 (m, 3H). The ^{1}H NMR spectral data are in good agreement with the literature data.[18]

*1-Nitro-4-(phenylethynyl)benzene (**3h**).* Following general procedure (**I**), substrate **3h** was obtained as a white solid (0.83 g, 80% yield), mp 120−122 °C. R_f = 0.30 on silica gel (petroleum ether). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.24−8.20 (m, 2H), 7.68−7.65 (m, 2H), 7.59−7.54 (m, 2H), 7.42−7.37 (m, 3H). The ^{1}H NMR spectral data are in good agreement with the literature data.[20]

*1-(4-(Phenylethynyl)phenyl)ethan-1-one (**3i**).* Following general procedure (**I**), substrate **3i** was obtained as a white solid (0.85 g, 85% yield), mp 97−99 °C. R_f = 0.25 on silica gel (ethyl acetate/petroleum ether 1:60, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.97−7.91 (m, 2H), 7.64−7.59 (m, 2H), 7.58−7.52 (m, 2H), 7.40−7.33 (m, 3H), 2.61 (s, 3H). The ^{1}H NMR spectral data are in good agreement with the literature data.[19]

*4-(Phenylethynyl)benzonitrile (**3j**).* Following general procedure (**I**), substrate **3j** was obtained as a white solid (0.81 g, 88% yield), mp 105−107 °C. R_f = 0.25 on silica gel (ethyl acetate/petroleum ether 1:60, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.65−7.59 (m, 4H), 7.57−7.52 (m, 2H), 7.42−7.35 (m, 3H). The ^{1}H NMR spectral data are in good agreement with the literature data.[21]

*1,2-Bis(4-fluorophenyl)ethyne (**3k**).* Following general procedure (**I**), substrate **3k** was obtained as a white solid (0.67 g, 80% yield), mp 91−93 °C. R_f = 0.92 on silica gel (petroleum ether). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.53−7.48 (m, 4H), 7.08−7.01 (m, 4H). The ^{1}H NMR spectral data are in good agreement with the literature data.[22]

*1,2-Di-p-tolylethyne (**3l**).* Following general procedure (**I**), substrate **3l** was obtained as a white solid (0.80 g, 86% yield), mp 117−119 °C. R_f = 0.91 on silica gel (petroleum ether). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.48−7.45 (m, 4H), 7.18 (d, J = 7.9 Hz, 4H), 2.40 (s, 6H). The ^{1}H NMR spectral data are in good agreement with the literature data.[23]

*2-(Phenylethynyl)thiophene (**3m**).* Following general procedure (**I**), substrate **3m** was obtained as a white solid (0.58 g, 70% yield), mp 52−54 °C. R_f = 0.89 on silica gel (petroleum ether). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.55−7.53 (m, 2H), 7.37−7.35 (m, 3H), 7.33−7.28 (m, 2H), 7.03 (dd, J = 5.0, 3.8 Hz, 1H). The ^{1}H NMR spectral data are in good agreement with the literature data.[24]

General Procedure (II) for Oxidation of C4-Alkynylisoxazoles into C4-(1,2-Diketoaryl)isoxazoles (2). C4-alkynylisoxazole **1** (0.125 mmol, 1 equiv) and $AgNO_3$ (42.5 mg, 2 equiv) were simultaneously added to a 10 mL round-bottomed flask, followed by

DOI: 10.1021/acs.joc.9b01667
J. Org. Chem. XXXX, XXX, XXX−XXX

the addition of MeCN (1.5 mL). Then ICl (0.25 M MeCN, 1 equiv) was added dropwise and the solution was allowed to stir at room temperature for 4 h under an air atmosphere. After the reaction was completed, the reaction was poured into 10 mL ethyl acetate and washed three times (3 × 10 mL) with brine. The organic layers were combined, dried with anhydrous $MgSO_4$, and then filtered. The filtrate was concentrated under vacuum, and the resulting residue was purified by using a TLC silica gel preparative plate using ethyl acetate/petroleum ether as the developing solvents to afford the desired products **2**.

*1-(3,5-Diphenylisoxazol-4-yl)-2-(p-tolyl)ethane-1,2-dione (**2a**).* Following general procedure (**II**), product **2a** was obtained as a yellow solid (37.7 mg, 82% yield), mp 100−102 °C. R_f = 0.30 on silica gel (ethyl acetate/petroleum ether 1:20, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.88 (d, J = 7.9 Hz, 2H), 7.67 (d, J = 8.2 Hz, 2H), 7.50 (t, J = 7.4 Hz, 3H), 7.41 (t, J = 7.7 Hz, 2H), 7.34 (t, J = 7.5 Hz, 1H), 7.26 (dd, J = 9.5, 5.7 Hz, 2H), 7.19 (d, J = 8.1 Hz, 2H), 2.41 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 190.1, 188.2, 175.1, 163.6, 145.9, 132.1, 130.3, 130.2, 130.1, 129.6, 129.4, 129.3, 128.8, 128.6, 127.8, 126.4, 113.7, 22.1. HRMS (ESI-ion trap) m/z: [M + H]$^+$ calcd for $C_{24}H_{18}NO_3$, 368.1287; found, 368.1285.

*1-(3-(tert-Butyl)-5-phenylisoxazol-4-yl)-2-(p-tolyl)ethane-1,2-dione (**2b**).* Following general procedure (**II**), product **2b** was obtained as a yellow solid (31.7 mg, 73% yield), mp 107−109 °C. R_f = 0.28 on silica gel (ethyl acetate/petroleum ether 1:30, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.64 (d, J = 8.1 Hz, 2H), 7.30 (t, J = 8.5 Hz, 3H), 7.19 (d, J = 7.9 Hz, 2H), 7.12 (t, J = 7.6 Hz, 2H), 2.40 (s, 3H), 1.52 (s, 9H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 190.4, 189.6, 176.7, 170.7, 145.7, 131.4, 130.6, 130.0, 129.5, 129.3, 128.5, 126.7, 113.8, 33.9, 28.4, 22.1. HRMS (ESI-ion trap) m/z: [M + H]$^+$ calcd for $C_{22}H_{22}NO_3$, 348.1600; found, 348.1593.

*1-(3-Isopropyl-5-phenylisoxazol-4-yl)-2-(p-tolyl)ethane-1,2-dione (**2c**).* Following general procedure (**II**), product **2c** was obtained as a yellow solid (28.9 mg, 70% yield), mp 108−110 °C. R_f = 0.30 on silica gel (ethyl acetate/petroleum ether 1:20, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.60 (d, J = 8.2 Hz, 2H), 7.30 (dd, J = 10.5, 4.3 Hz, 3H), 7.17−7.12 (m, 4H), 3.43 (hept, J = 6.9 Hz, 1H), 2.35 (s, 3H), 1.35 (d, J = 6.9 Hz, 6H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 190.8, 189.3, 175.9, 169.2, 146.1, 131.6, 130.4, 130.1, 129.7, 129.4, 128.6, 126.6, 112.8, 27.1, 22.1, 21.2. HRMS (ESI-ion trap) m/z: [M + H]$^+$ calcd for $C_{21}H_{20}NO_3$, 334.1443; found, 334.1441.

*1-(5-(tert-Butyl)-3-phenylisoxazol-4-yl)-2-(p-tolyl)ethane-1,2-dione (**2d**).* Following general procedure (**II**), product **2d** was obtained as a yellow solid (33.8 mg, 78% yield), mp 102−104 °C. R_f = 0.30 on silica gel (ethyl acetate/petroleum ether 1:30, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.63 (d, J = 8.2 Hz, 2H), 7.26−7.24 (m, 2H), 7.23−7.16 (m, 3H), 7.09 (t, J = 7.7 Hz, 2H), 2.41 (d, J = 7.8 Hz, 3H), 1.54 (s, 9H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 190.2, 189.4, 185.5, 163.4, 145.8, 130.2, 130.1, 130.0, 129.5, 129.3, 128.5, 128.1, 113.4, 35.6, 27.9, 22.1. HRMS (ESI-ion trap) m/z: [M + H]$^+$ calcd for $C_{22}H_{22}NO_3$, 348.1600; found, 348.1601.

*1-(5-Cyclopropyl-3-phenylisoxazol-4-yl)-2-(p-tolyl)ethane-1,2-dione (**2e**).* Following general procedure (**II**), product **2e** was obtained as a yellow oil (29.4 mg, 71% yield). R_f = 0.28 on silica gel (ethyl acetate/petroleum ether 1:25, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.68 (d, J = 8.2 Hz, 2H), 7.35−7.31 (m, 3H), 7.24−7.19 (m, 4H), 2.72 (tt, J = 8.4, 5.0 Hz, 1H), 2.43 (s, 3H), 1.42−1.39 (m, 2H), 1.27−1.24 (m, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 191.5, 188.9, 182.1, 162.8, 146.2, 130.2, 130.2, 130.1, 129.7, 129.3, 128.4, 127.7, 113.9, 22.1, 11.3, 9.7. HRMS (ESI-ion trap) m/z: [M + H]$^+$ calcd for $C_{21}H_{18}NO_3$, 332.1287; found, 332.1281.

*1-(5-Pentyl-3-phenylisoxazol-4-yl)-2-(p-tolyl)ethane-1,2-dione (**2f**).* Following general procedure (**II**), product **2f** was obtained as a yellow oil (33.8 mg, 78% yield). R_f = 0.30 on silica gel (ethyl acetate/petroleum ether 1:35, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.69 (d, J = 8.2 Hz, 2H), 7.40−7.36 (m, 2H), 7.35−7.32 (m, 1H), 7.23 (dt, J = 13.7, 7.0 Hz, 4H), 3.07−3.03 (m, 2H), 2.42 (s, 3H), 1.79 (dt, J = 15.3, 7.6 Hz, 2H), 1.37−1.32 (m, 4H), 0.89 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 191.1, 188.7, 181.3, 162.5, 146.3, 130.2, 130.1, 130.0, 129.8, 129.3, 128.4, 127.8, 113.5, 31.5, 27.8, 27.1, 22.3, 22.1, 14.0. HRMS (ESI-ion trap) m/z: [M + H]$^+$ calcd for $C_{23}H_{24}NO_3$, 362.1756; found, 362.1754.

*1-(5-(tert-Butyl)-3-(4-methoxyphenyl)isoxazol-4-yl)-2-(p-tolyl)-ethane-1,2-dione (**2g**).* Following general procedure (**II**), product **2g** was obtained as a yellow solid (35.8 mg, 76% yield), mp 102−104 °C. R_f = 0.28 on silica gel (ethyl acetate/petroleum ether 1:15, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.56 (d, J = 8.0 Hz, 2H), 7.09 (dd, J = 15.5, 8.2 Hz, 4H), 6.50 (d, J = 8.5 Hz, 2H), 3.58 (s, 3H), 2.32 (s, 3H), 1.45 (s, 9H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 190.4, 189.6, 185.3, 163.1, 160.9, 145.7, 130.7, 130.2, 129.4, 120.2, 113.9, 113.5, 55.3, 35.5, 27.9, 22.0. HRMS (ESI-ion trap) m/z: [M + H]$^+$ calcd for $C_{23}H_{24}NO_4$, 378.1705; found, 378.1703.

*1-(5-(tert-Butyl)-3-(4-(trifluoromethyl)phenyl)isoxazol-4-yl)-2-(p-tolyl)ethane-1,2-dione (**2h**).* Following general procedure (**II**), product **2h** was obtained as a yellow oil (33.7 mg, 65% yield). R_f = 0.30 on silica gel (ethyl acetate/petroleum ether 1:35, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.58 (d, J = 7.9 Hz, 2H), 7.37−7.31 (m, 4H), 7.17 (d, J = 7.9 Hz, 2H), 2.41 (s, 3H), 1.55 (s, 9H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 190.5, 188.9, 185.8, 162.3, 146.4, 131.9 (q, J = 33.0 Hz), 131.6, 130.0, 129,9, 129,8 129.6, 125.3 (q, J = 4.5 Hz), 123.7 (q, J = 270.0 Hz), 113.5, 35.6, 27.9, 22.1. HRMS (ESI-ion trap) m/z: [M + H]$^+$ calcd for $C_{23}H_{21}F_3NO_3$, 416.1474; found, 416.1470.

*1-(5-(tert-Butyl)-3-(4-(trifluoromethyl)phenyl)isoxazol-4-yl)-2-(4-methoxyphenyl)ethane-1,2-dione (**2i**).* Following general procedure (**II**), product **2i** was obtained as a yellow solid (37.7 mg, 70% yield), mp 83−85 °C. R_f = 0.30 on silica gel (ethyl acetate/petroleum ether 1:15, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.69−7.64 (m, 2H), 7.36 (s, 4H), 6.87−6.83 (m, 2H), 3.88 (s, 3H), 1.55 (s, 9H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 189.3, 189.1, 185.7, 165.1, 162.3, 132.4, 131.9 (q, J = 33.0 Hz), 131.8, 125.4, 125.2 (q, J = 3.0 Hz), 123.8 (q, J = 271.5 Hz), 114.3, 113.6, 55.8, 35.6, 27.9. ^{19}F NMR (564 MHz, $CDCl_3$): δ −63.11. HRMS (ESI-ion trap) m/z: [M + H]$^+$ calcd for $C_{23}H_{21}F_3NO_4$, 432.1423; found, 432.1421.

*1-(3,5-Diphenylisoxazol-4-yl)-2-phenylethane-1,2-dione (**2j**).* Following general procedure (**II**), product **2j** was obtained as a yellow solid (33.1 mg, 75% yield), mp 111−113 °C. R_f = 0.29 on silica gel (ethyl acetate/petroleum ether 1:20, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.86−7.79 (m, 2H), 7.68 (dd, J = 8.2, 1.1 Hz, 2H), 7.50 (t, J = 7.4 Hz, 1H), 7.42 (dd, J = 12.0, 4.3 Hz, 3H), 7.32 (dt, J = 15.5, 7.9 Hz, 4H), 7.25 (t, J = 7.5 Hz, 1H), 7.17 (dd, J = 8.7, 6.6 Hz, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 190.4, 188.1, 175.2, 163.6, 134.7, 132.7, 132.3, 130.4, 130.1, 129.4, 129.3, 128.9, 128.8, 128.6, 127.7, 126.4, 113.7. HRMS (ESI-ion trap) m/z: [M + H]$^+$ calcd for $C_{23}H_{16}NO_3$, 354.1130; found, 354.1120.

*1-(3,5-Diphenylisoxazol-4-yl)-2-(4-fluorophenyl)ethane-1,2-dione (**2k**).* Following general procedure (**II**), product **2k** was obtained as a yellow solid (23.1 mg, 50% yield), mp 160−162 °C. R_f = 0.28 on silica gel (ethyl acetate/petroleum ether 1:25, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95−7.86 (m, 2H), 7.85−7.75 (m, 2H), 7.48 (ddd, J = 21.1, 15.1, 7.4 Hz, 5H), 7.35 (t, J = 7.4 Hz, 1H), 7.27 (t, J = 7.4 Hz, 2H), 7.08 (t, J = 8.6 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 188.8, 187.7, 175.3, 166.7 (d, J = 257.0 Hz), 163.5, 132.8 (d, J = 10.0 Hz), 132.3, 130.4, 129.4 (d, J = 8.0 Hz), 129.2 (d, J = 3.0 Hz), 128.9, 128.6, 127.7, 126.3, 116.3, 116.1, 113.6. HRMS (ESI-ion trap) m/z: [M + H]$^+$ calcd for $C_{23}H_{15}FNO_3$, 372.1036; found, 372.1033.

*1-(3,5-Diphenylisoxazol-4-yl)-2-(m-tolyl)ethane-1,2-dione (**2l**).* Following general procedure (**II**), product **2l** was obtained as a yellow solid (36.3 mg, 79% yield), mp 98−100 °C. R_f = 0.30 on silica gel (ethyl acetate/petroleum ether 1:30, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, J = 7.2 Hz, 2H), 7.56 (d, J = 7.6 Hz, 1H), 7.53−7.48 (m, 4H), 7.41 (dd, J = 15.2, 7.7 Hz, 3H), 7.35 (d, J = 7.4 Hz, 1H), 7.27 (d, J = 8.1 Hz, 3H), 2.34 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 190.7, 188.1, 175.2, 163.5, 135.5, 132.2, 130.3, 130.3, 129.5, 129.4, 128.9, 128.7, 128.6, 127.3, 113.7, 21.4. HRMS (ESI-ion trap) m/z: [M + H]$^+$ calcd for $C_{24}H_{18}NO_3$, 368.1287; found, 368.1287.

*1-(3,5-Diphenylisoxazol-4-yl)-2-(4-methoxyphenyl)ethane-1,2-dione (**2m**).* Following general procedure (**II**), product **2m** was obtained as a yellow solid (37.4 mg, 78% yield), mp 90−92 °C. R_f =

DOI: 10.1021/acs.joc.9b01667
J. Org. Chem. XXXX, XXX, XXX−XXX

0.25 on silica gel (ethyl acetate/petroleum ether 1:8, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.87 (d, J = 7.8 Hz, 2H), 7.75 (d, J = 8.8 Hz, 2H), 7.49 (dd, J = 11.3, 7.6 Hz, 3H), 7.40 (t, J = 7.7 Hz, 2H), 7.33 (d, J = 7.2 Hz, 1H), 7.26 (t, J = 7.5 Hz, 2H), 6.85 (d, J = 8.8 Hz, 2H), 3.85 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 188.9, 188.3, 174.9, 164.8, 163.5, 132.5, 132.1, 130.2, 129.4, 129.3, 128.8, 128.5, 127.8, 126.4, 125.8, 114.1, 55.7. HRMS (ESI-ion trap) m/z: [M + H]$^+$ calcd for $C_{24}H_{18}NO_4$, 384.1236; found, 384.1234.

*1-(4-(tert-Butyl)phenyl)-2-(3,5-diphenylisoxazol-4-yl)ethane-1,2-dione (**2n**).* Following general procedure (**II**), product **2n** was obtained as a yellow solid (30.7 mg, 78% yield), mp 131−133 °C. R_f = 0.30 on silica gel (ethyl acetate/petroleum ether 1:25, v/v). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, J = 7.3 Hz, 2H), 7.61 (d, J = 8.6 Hz, 2H), 7.46−7.39 (m, 3H), 7.33 (t, J = 7.6 Hz, 4H), 7.25 (t, J = 7.4 Hz, 1H), 7.16 (t, J = 7.4 Hz, 2H), 1.25 (s, 9H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 190.1, 188.3, 175.1, 163.5, 158.8, 132.2, 130.3, 130.2, 130.0, 129.4, 129.3, 128.8, 128.5, 127.7, 126.4, 125.8, 113.7, 35.5, 31.2. HRMS (ESI-ion trap) m/z: [M + H]$^+$ calcd for $C_{27}H_{24}NO_3$, 410.1756; found, 410.1754.

General Procedure (III) for Oxidation of Alkynes into 1,2-Diketones (4). Alkynes **3** (0.15 mmol, 1 equiv) and $AgNO_3$ (76.4 mg, 3 equiv) were simultaneously added to a 10 mL round-bottomed flask, followed by the addition of MeCN (1.5 mL). Then ICl (0.15 M MeCN, 0.5 equiv) was added dropwise and the solution was allowed to stir at room temperature for 4 h under an air atmosphere. After the reaction was completed as judged by TLC, the reaction mixture was poured into 10 mL ethyl acetate and washed three times (3 × 10 mL) with brine. The organic layers were combined, dried with anhydrous $MgSO_4$, and then filtered. The filtrate was concentrated under vacuum, and the resulting residue was purified by using a TLC silica gel preparative plate using ethyl acetate/petroleum ether as the developing solvents to afford the desired products **4**.

*Benzil (**4a**).* Following general procedure (**III**), product **4a** was obtained as a yellow solid (28.3 mg, 90% yield), mp 93−95 °C. R_f = 0.30 on silica gel (ethyl acetate/petroleum ether 1:20, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.98 (d, J = 7.6 Hz, 4H), 7.66 (t, J = 7.4 Hz, 2H), 7.51 (t, J = 7.8 Hz, 4H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 194. 8, 135.1, 133.2, 130.1, 129.2. HRMS (ESI-ion trap) m/z: [M + H]$^+$ calcd for $C_{14}H_{11}O_2$, 211.0759; found, 211.0755.

*1-(4-Methoxyphenyl)-2-phenylethane-1,2-dione (**4b**).* Following general procedure (**III**), product **4b** was obtained as a yellow solid (21.6 mg, 60% yield), mp 60−62 °C. R_f = 0.27 on silica gel (ethyl acetate/petroleum ether 1:15, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.99−7.92 (m, 4H), 7.66−7.62 (m, 1H), 7.52−7.48 (m, 2H), 6.99−6.96 (m, 2H), 3.88 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 195.1, 193.4, 165.2, 134.9, 133.4, 132.6, 130.1, 129.2, 126.3, 114.6, 55.9. HRMS (ESI-ion trap) m/z: [M + H]$^+$ calcd for $C_{15}H_{13}O_3$, 241.0865; found, 241.0864.

*1-Phenyl-2-(p-tolyl)ethane-1,2-dione (**4c**).* Following general procedure (**III**), product **4c** was obtained as a yellow solid (29.6 mg, 88% yield), mp 93−95 °C. R_f = 0.30 on silica gel (ethyl acetate/petroleum ether 1:20, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.99−7.94 (m, 2H), 7.87 (d, J = 8.2 Hz, 2H), 7.64 (q, J = 7.4 Hz, 1H), 7.50 (t, J = 7.8 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 2.43 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 194.9, 194.5, 146.4, 134.9, 133.3, 130.8, 130.2, 130.1, 129.9, 129.2, 22.2. HRMS (ESI-ion trap) m/z: [M + H]$^+$ calcd for $C_{15}H_{13}O_2$, 225.0916; found, 225.0910.

*1-(4-Fluorophenyl)-2-phenylethane-1,2-dione (**4d**).* Following general procedure (**III**), product **4d** was obtained as a yellow solid (29.4 mg, 86% yield), mp 63−65 °C. R_f = 0.30 on silica gel (ethyl acetate/petroleum ether 1:25, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.04−8.00 (m, 2H), 7.97 (dd, J = 8.3, 1.1 Hz, 2H), 7.69−7.64 (m, 1H), 7.52 (t, J = 7.9 Hz, 2H), 7.22−7.16 (m, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 194.3, 192.9, 166.6 (d, J = 255.0 Hz), 135.2, 133.1, 132.9 (d, J = 15.0 Hz), 130.1, 129.6 (d, J = 15.0 Hz), 129.3, 116.6 (d, J = 30.0 Hz). HRMS (ESI-ion trap) m/z: [M + H]$^+$ calcd for $C_{14}H_{10}FO_2$, 229.0665; found, 229.0655.

*1-(4-Chlorophenyl)-2-phenylethane-1,2-dione (**4e**).* Following general procedure (**III**), product **4e** was obtained as a yellow solid (31.8 mg, 87% yield), mp 73−75 °C. R_f = 0.30 on silica gel (ethyl acetate/petroleum ether 1:30, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.99−7.94 (m, 2H), 7.87−7.82 (m, 2H), 7.69−7.64 (m, 3H), 7.54−7.50 (m, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 194.1, 193.5, 135.3, 132.9, 132.6, 131.9, 131.4, 130.7, 130.2, 129.3. HRMS (ESI-ion trap) m/z: [M − Cl]$^+$ calcd for $C_{14}H_9O_2$, 209.0603; found, 209.0609.

*1-(4-Bromophenyl)-2-phenylethane-1,2-dione (**4f**).* Following general procedure (**III**), product **4f** was obtained as a yellow solid (33.7 mg, 78% yield), mp 85−87 °C. R_f = 0.30 on silica gel (ethyl acetate/petroleum ether 1:35, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.96 (dd, J = 8.3, 1.1 Hz, 2H), 7.94−7.90 (m, 2H), 7.69−7.65 (m, 1H), 7.54−7.47 (m, 4H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 194.1, 193.3, 141.8, 135.3, 132.9, 131.6, 131.4, 130.2, 129.6, 129.3. HRMS (ESI-ion trap) m/z: [M + H]$^+$ calcd for $C_{14}H_{10}BrO_2$, 288.9864; found, 288.9863.

*1-Phenyl-2-(4-(trifluoromethyl)phenyl)ethane-1,2-dione (**4g**).* Following general procedure (**III**), product **4g** was obtained as a yellow solid (36.2 mg, 87% yield), mp 88−90 °C. R_f = 0.30 on silica gel (ethyl acetate/petroleum ether 1:30, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.11 (d, J = 8.2 Hz, 2H), 7.98 (dd, J = 8.2, 1.1 Hz, 2H), 7.78 (d, J = 8.3 Hz, 2H), 7.69 (t, J = 7.5 Hz, 1H), 7.54 (t, J = 7.8 Hz, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 193.7, 193.2, 136.1 (q, J = 33.0 Hz), 135.8, 135.5, 132.8, 130.4, 130.2, 129.4, 126.3 (q, J = 4.5 Hz), 123.5 (q, J = 271.5 Hz). HRMS (ESI-ion trap) m/z: [M + H]$^+$ calcd for $C_{15}H_{10}F_3O_2$, 279.0633; found, 279.0633.

*1-(4-Nitrophenyl)-2-phenylethane-1,2-dione (**4h**).* Following general procedure (**III**), product **4h** was obtained as a yellow solid (29.8 mg, 78% yield), mp 125−127 °C. R_f = 0.26 on silica gel (ethyl acetate/petroleum ether 1:15, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.37−8.32 (m, 2H), 8.19−8.14 (m, 2H), 8.02−7.95 (m, 2H), 7.71 (ddd, J = 7.8, 2.5, 1.2 Hz, 1H), 7.58−7.52 (m, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 193.1, 192.3, 151.4, 137.5, 135.7, 132.6, 131.2, 130.3, 129.4, 124.3. HRMS (ESI-ion trap) m/z: [M + H]$^+$ calcd for $C_{14}H_{10}NO_4$, 256.0610; found, 256.0600.

*1-(4-Acetylphenyl)-2-phenylethane-1,2-dione (**4i**).* Following general procedure (**III**), product **4i** was obtained as a yellow solid (30.9 mg, 81% yield), mp 75−77 °C. R_f = 0.29 on silica gel (ethyl acetate/petroleum ether 1:15, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.05 (s, 4H), 7.97−7.94 (m, 2H), 7.68−7.65 (m, 1H), 7.53−7.50 (m, 2H), 2.63 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 197.5, 193.9, 193.8, 141.4, 136.1, 135.4, 132.8, 130.3, 130.1, 129.3, 128.9, 27.1. HRMS (ESI-ion trap) m/z: [M + H]$^+$ calcd for $C_{16}H_{13}O_3$, 253.0865; found, 253.0861.

*4-(2-Oxo-2-phenylacetyl)benzonitrile (**4j**).* Following general procedure (**III**), product **4j** was obtained as a yellow solid (30.6 mg, 87% yield), mp 110−112 °C. R_f = 0.29 on silica gel (ethyl acetate/petroleum ether 1:25, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.08 (d, J = 8.2 Hz, 2H), 7.97 (d, J = 7.6 Hz, 2H), 7.81 (d, J = 8.2 Hz, 2H), 7.70 (t, J = 7.4 Hz, 1H), 7.54 (t, J = 7.7 Hz, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 193.2, 192.6, 136.1, 135.6, 132.9, 132.6, 130.4, 130.2, 129.4, 118.1, 117.8. HRMS (ESI-ion trap) m/z: [M + H]$^+$ calcd for $C_{15}H_{10}NO_2$, 236.0712; found, 236.0711.

*1,2-Bis(4-fluorophenyl)ethane-1,2-dione (**4k**).* Following general procedure (**III**), product **4k** was obtained as a yellow solid (31.7 mg, 86% yield), mp 118−120 °C. R_f = 0.30 on silica gel (ethyl acetate/petroleum ether 1:40, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.05−7.99 (m, 4H), 7.22−7.17 (m, 4H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 192.5, 167.1 (d, J = 258.0 Hz), 133.1 (d, J = 9.0 Hz), 129.6 (d, J = 3.0 Hz), 116.7 (d, J = 22.5 Hz). ^{19}F NMR (564 MHz, $CDCl_3$): δ −100.92. HRMS (ESI-ion trap) m/z: [M + H]$^+$ calcd for $C_{14}H_9F_2O_2$, 247.0571; found, 247.0570.

*1,2-Di-p-tolylethane-1,2-dione (**4l**).* Following general procedure (**III**), product **4l** was obtained as a yellow solid (30.0 mg, 84% yield), mp 101−103 °C. R_f = 0.28 on silica gel (ethyl acetate/petroleum ether 1:50, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.89−7.82 (m, 4H), 7.30 (dd, J = 8.5, 0.5 Hz, 4H), 2.43 (s, 6H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 194.7, 146.3, 130.9, 130.2, 129.9, 22.1. HRMS (ESI-ion trap) m/z: [M + H]$^+$ calcd for $C_{16}H_{15}O_2$, 239.1072; found, 239.1071.

*1-Phenyl-2-(thiophen-2-yl)ethane-1,2-dione (**4m**).* Following general procedure (**III**), product **4m** was obtained as a yellow oil

DOI: 10.1021/acs.joc.9b01667
J. Org. Chem. XXXX, XXX, XXX−XXX

(28.1 mg, 87% yield). R_f = 0.29 on silica gel (ethyl acetate/petroleum ether 1:50, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.04 (dd, J = 8.2, 1.1 Hz, 2H), 7.84 (dd, J = 4.8, 1.0 Hz, 1H), 7.81−7.78 (m, 1H), 7.65 (dd, J = 11.7, 4.3 Hz, 1H), 7.51 (t, J = 7.8 Hz, 2H), 7.18 (dd, J = 4.8, 4.0 Hz, 1H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 192.3, 185.8, 140.1, 137.1, 136.9, 135.1, 132.8, 130.4, 129.1, 129.0. HRMS (ESI-ion trap) m/z: $[M + H]^+$ calcd for $C_{12}H_9O_2S$, 217.0323; found, 217.0320.

*1-Phenylbutane-1,2-dione (**4n**).* Following general procedure (**III**), product **4n** was obtained as a yellow oil (18.2 mg, 75% yield). R_f = 0.28 on silica gel (ethyl acetate/petroleum ether 1:80, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.98 (dt, J = 8.4, 1.4 Hz, 2H), 7.65−7.62 (m, 1H), 7.51−7.47 (m, 2H), 2.91 (q, J = 7.3 Hz, 2H), 1.20 (t, J = 7.3 Hz, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 204.1, 192.8, 134.8, 132.2, 130.3, 129.1, 32.3, 7.0. HRMS (ESI-ion trap) m/z: $[M + H]^+$ calcd for $C_{10}H_{11}O_2$, 163.0759; found, 163.0754.

Procedure (IV) for Synthesis of 5. C4-(1,2-Diketoaryl)-isoxazoles **2** (0.15 mmol, 1 equiv), 1,2-diaminobenzene (0.18 mmol, 19.5 mg) and MeCN (2.5 mL) were simultaneously added to a 10 mL round-bottomed flask. Then the solution was allowed to stir at room temperature for 6 h under an air atmosphere. After the reaction was completed as judged by TLC, the reaction mixture was poured into 10 mL ethyl acetate and washed three times (3 × 10 mL) with brine. The organic layers were combined, dried with anhydrous $MgSO_4$, and then filtered. The filtrate was concentrated under vacuum, and the resulting residue was purified by using a TLC silica gel preparative plate using ethyl acetate/petroleum ether as the developing solvents to afford the desired products **5**.

*3,5-Diphenyl-4-(3-(p-tolyl)quinoxalin-2-yl)isoxazole (**5a**).* Following procedure (**IV**), product **5a** was obtained as a white solid (54.1 mg, 82% yield). mp 163−165 °C. R_f = 0.25 on silica gel (ethyl acetate/petroleum ether 1:20, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.19 (td, J = 8.1, 1.6 Hz, 2H), 7.87−7.78 (m, 2H), 7.63−7.57 (m, 2H), 7.42−7.35 (m, 1H), 7.34−7.26 (m, 3H), 7.21−7.11 (m, 4H), 6.97−6.87 (m, 4H), 2.28 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 168.1, 162.7, 155.2, 145.7, 141.8, 141.2, 138.8, 134.7, 130.9, 130.5, 130.3, 129.6, 129.5, 129.3, 128.9, 128.8, 128.7, 128.6, 128.5, 127.9, 127.5, 127.2, 114.3, 21.3. HRMS (ESI-ion trap) m/z: $[M + H]^+$ calcd for $C_{30}H_{22}N_3O$, 440.1763; found, 440.1761.

*3-Isopropyl-5-phenyl-4-(3-(p-tolyl)quinoxalin-2-yl)isoxazole (**5b**).* Following procedure (**IV**), product **5b** was obtained as a white solid (47.6 mg, 98% yield). mp 129−131 °C. R_f = 0.25 on silica gel (ethyl acetate/petroleum ether 1:20, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.23−8.13 (m, 2H), 7.82 (pd, J = 6.9, 1.7 Hz, 2H), 7.28 (ddd, J = 8.7, 6.0, 3.0 Hz, 1H), 7.21−7.16 (m, 4H), 7.14 (d, J = 8.1 Hz, 2H), 6.96 (d, J = 7.9 Hz, 2H), 3.02 (hept, J = 6.9 Hz, 1H), 2.27 (s, 3H), 1.31 (d, J = 6.9 Hz, 3H), 1.14 (d, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 168.5, 167.2, 154.7, 145.8, 141.8, 141.3, 139.1, 134.9, 130.8, 130.3, 130.2, 129.6, 129.3, 129.0, 128.9, 128.6, 127.7, 127.1, 113.8, 26.5, 21.5, 21.3, 21.2. HRMS (ESI-ion trap) m/z: $[M + H]^+$ calcd for $C_{27}H_{24}N_3O$, 406.1919; found, 406.1919.

*5-Cyclopropyl-3-phenyl-4-(3-(p-tolyl)quinoxalin-2-yl)isoxazole (**5c**).* Following procedure (**IV**), product **5c** was obtained as a yellow oil (50.8 mg, 84% yield). R_f = 0.26 on silica gel (ethyl acetate/petroleum ether 1:20, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.23−8.13 (m, 2H), 7.84−7.75 (m, 2H), 7.26−7.21 (m, 1H), 7.13−7.08 (m, 2H), 7.04 (d, J = 8.1 Hz, 2H), 7.01−6.92 (m, 4H), 2.31 (s, 3H), 2.18 (ddd, J = 16.9, 8.2, 5.3 Hz, 1H), 1.12 (t, J = 124.3 Hz, 4H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 173.2, 161.9, 154.9, 145.5, 141.7, 141.3, 138.8, 135.2, 130.6, 130.1, 129.5, 129.3, 129.2, 128.9, 128.4, 127.7, 114.4, 21.4, 8.2. HRMS (ESI-ion trap) m/z: $[M + H]^+$ calcd for $C_{27}H_{22}N_3O$, 404.1763; found, 404.1763.

*3,5-Diphenyl-4-(3-phenylquinoxalin-2-yl)isoxazole (**5d**).* Following procedure (**IV**), product **5d** was obtained as a yellow oil (61.2 mg, 96% yield). R_f = 0.20 on silica gel (ethyl acetate/petroleum ether 1:20, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.20 (ddd, J = 7.5, 5.5, 1.9 Hz, 2H), 7.89−7.82 (m, 2H), 7.58 (d, J = 7.5 Hz, 2H), 7.42−7.36 (m, 1H), 7.35−7.28 (m, 3H), 7.23−7.19 (m, 1H), 7.17 (dd, J = 10.7, 4.9 Hz, 2H), 7.09 (dd, J = 15.7, 7.8 Hz, 4H), 7.00 (d, J = 8.1 Hz, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 168.2, 162.7, 155.1, 145.7, 141.9, 141.4, 137.6, 131.1, 130.6, 130.5, 129.7, 129.6, 129.4, 129.0, 128.9, 128.8, 128.7, 128.6, 128.1, 128.0, 127.5, 127.3, 114.2. HRMS (ESI-ion trap) m/z: $[M + H]^+$ calcd for $C_{29}H_{20}N_3O$, 426.1606; found, 426.1606.

*4-(3-(4-Fluorophenyl)quinoxalin-2-yl)-3,5-diphenylisoxazole (**5e**).* Following procedure (**IV**), product **5e** was obtained as a yellow oil (55.8 mg, 84% yield). R_f = 0.23 on silica gel (ethyl acetate/petroleum ether 1:20, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.23−8.15 (m, 2H), 7.91−7.82 (m, 2H), 7.59 (dd, J = 5.2, 3.4 Hz, 2H), 7.43−7.38 (m, 1H), 7.37−7.28 (m, 3H), 7.18 (dd, J = 10.7, 4.9 Hz, 2H), 7.11 (dd, J = 8.2, 1.2 Hz, 2H), 7.03−6.96 (m, 2H), 6.84−6.74 (m, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 168.3, 163.2 (d, J = 249.0 Hz), 162.7, 154.0, 145.5, 141.8, 141.5, 133.8 (d, J = 3.0 Hz), 131.3, 130.9 (d, J = 7.5 Hz), 130.7 (d, J = 12.0 Hz), 129.8, 129.6, 129.5, 129.1, 128.8, 128.7, 128.0, 127.5, 127.3, 115.3 (d, J = 21.0 Hz), 114.0. ^{19}F NMR (564 MHz, $CDCl_3$): δ −112.01. HRMS (ESI-ion trap) m/z: $[M + H]^+$ calcd for $C_{29}H_{19}FN_3O$, 444.1512; found, 444.1512.

*3,5-Diphenyl-4-(3-(m-tolyl)quinoxalin-2-yl)isoxazole (**5f**).* Following procedure (**IV**), product **5f** was obtained as a white solid (61.3 mg, 93% yield). mp 167−169 °C. R_f = 0.25 on silica gel (ethyl acetate/petroleum ether 1:20, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.20 (dt, J = 4.9, 2.0 Hz, 2H), 7.89−7.81 (m, 2H), 7.62−7.56 (m, 2H), 7.40 (t, J = 7.4 Hz, 1H), 7.35−7.29 (m, 3H), 7.18 (t, J = 7.8 Hz, 2H), 7.11 (dd, J = 8.1, 1.0 Hz, 2H), 7.03 (d, J = 7.6 Hz, 1H), 6.99 (t, J = 7.5 Hz, 1H), 6.79 (d, J = 7.5 Hz, 1H), 6.70 (s, 1H), 2.12 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 168.2, 162.7, 155.4, 145.8, 141.8, 141.3, 138.1, 137.5, 131.1, 130.5, 130.4, 129.8, 129.6, 129.5, 129.4, 129.3, 128.9, 128.7, 128.6, 128.1, 127.8, 127.5, 127.3, 125.7, 114.3, 21.4. HRMS (ESI-ion trap) m/z: $[M + H]^+$ calcd for $C_{30}H_{22}N_3O$, 440.1763; found, 440.1763.

*4-(3-(4-Methoxyphenyl)quinoxalin-2-yl)-3,5-diphenylisoxazole (**5g**).* Following procedure (**IV**), product **5g** was obtained as a white solid (65.5 mg, 96% yield). mp 176−178 °C. R_f = 0.21 on silica gel (ethyl acetate/petroleum ether 1:7, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.21−8.14 (m, 2H), 7.86−7.80 (m, 2H), 7.63−7.57 (m, 2H), 7.39 (dd, J = 8.3, 6.5 Hz, 1H), 7.35−7.27 (m, 3H), 7.16 (dd, J = 10.7, 4.9 Hz, 2H), 7.12 (d, J = 7.2 Hz, 2H), 7.00 (t, J = 5.7 Hz, 2H), 6.67−6.58 (m, 2H), 3.76 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 168.1, 162.8, 160.3, 154.7, 145.7, 141.9, 141.2, 131.0, 130.6, 130.4, 130.2, 130.1, 129.6, 129.5, 129.4, 128.9, 128.7, 128.6, 127.9, 127.5, 127.3, 114.4, 113.7, 55.5. HRMS (ESI-ion trap) m/z: $[M + H]^+$ calcd for $C_{30}H_{22}N_3O_2$, 456.1712; found, 456.1712.

*4-(3-(4-(tert-Butyl)phenyl)quinoxalin-2-yl)-3,5-diphenylisoxazole (**5h**).* Following procedure (**IV**), product **5h** was obtained as a yellow oil (68.6 mg, 95% yield). R_f = 0.30 on silica gel (ethyl acetate/petroleum ether 1:25, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.23−8.14 (m, 2H), 7.88−7.79 (m, 2H), 7.60 (d, J = 7.4 Hz, 2H), 7.39 (t, J = 7.4 Hz, 1H), 7.34−7.27 (m, 3H), 7.14 (t, J = 7.8 Hz, 2H), 7.10 (d, J = 8.3 Hz, 2H), 7.06 (d, J = 7.5 Hz, 2H), 6.93 (d, J = 8.3 Hz, 2H), 1.28 (s, 9H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 168.3, 162.8, 155.1, 151.9, 145.6, 141.9, 141.3, 134.6, 130.9, 130.6, 130.3, 129.6, 129.5, 129.4, 128.9, 128.8, 128.6, 128.6, 128.0, 127.6, 127.4, 125.2, 114.4, 34.7, 31.3. HRMS (ESI-ion trap) m/z: $[M + H]^+$ calcd for $C_{33}H_{28}N_3O$, 482.2232; found, 482.2232.

Procedure (V) for Synthesis of 6. 1,2-Diarylalkynes **3** (0.15 mmol, 1 equiv) and $AgNO_3$ (76.4 mg, 3 equiv) were simultaneously added to a 10 mL round-bottomed flask, followed by the addition of MeCN (1.5 mL). Then ICl (0.15 M in MeCN, 0.5 equiv) was added dropwise and the solution was allowed to stir at room temperature for 4 h under an air atmosphere. After the reaction was completed as judged by TLC, 1,2-diaminobenzene (0.18 mmol, 19.5 mg) was added to the reaction mixture directly. The mixture was stirred at room temperature for 4 h. Then the reaction mixture was poured into 10 mL ethyl acetate and washed three times (3 × 10 mL) with brine. The organic layers were combined, dried with anhydrous $MgSO_4$, and then filtered. The filtrate was concentrated under vacuum, and the resulting residue was purified by using a TLC silica gel preparative plate using ethyl acetate/petroleum ether as the developing solvents to afford the desired products **6**.

DOI: 10.1021/acs.joc.9b01667
J. Org. Chem. XXXX, XXX, XXX−XXX

*2,3-Diphenylquinoxaline (**6a**).* Following procedure (**V**), product **6a** was obtained as a yellow solid (41.1 mg, 73% yield). mp 119−121 °C. R_f = 0.27 on silica gel (ethyl acetate/petroleum ether 1:20, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.19 (dd, J = 6.4, 3.4 Hz, 2H), 7.81−7.74 (m, 2H), 7.56−7.50 (m, 4H), 7.40−7.30 (m, 6H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 153.7, 141.4, 139.2, 130.2, 130.1, 129.4, 129.0, 128.5. HRMS (ESI-ion trap) m/z: $[M + H]^+$ calcd for $C_{20}H_{15}N_2$, 283.1235; found, 283.1230.

*2,3-Bis(4-fluorophenyl)quinoxaline (**6b**).* Following procedure (**V**), product **6b** was obtained as a yellow solid (47.7 mg, 65% yield). mp 173−175 °C. R_f = 0.30 on silica gel (ethyl acetate/petroleum ether 1:30, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.15 (dd, J = 6.4, 3.4 Hz, 2H), 7.78 (dd, J = 6.4, 3.4 Hz, 2H), 7.54−7.47 (m, 4H), 7.09−7.01 (m, 4H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 163.4 (d, J = 247.5 Hz), 152.4, 141.4, 135.2 (d, J = 4.5 Hz), 131.9 (d, J = 9.0 Hz), 130.4, 129.3, 115.7 (d, J = 21.0 Hz). ^{19}F NMR (564 MHz, $CDCl_3$): δ −111.91. HRMS (ESI-ion trap) m/z: $[M + H]^+$ calcd for $C_{20}H_{12}F_2N_2$, 319.1047; found, 319.1047.

*2,3-Di-p-tolylquinoxaline (**6c**).* Following procedure (**V**), product **6c** was obtained as a yellow solid (46.5 mg, 60% yield). mp 169−171 °C. R_f = 0.30 on silica gel (ethyl acetate/petroleum ether 1:35, v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.16 (dd, J = 6.3, 3.4 Hz, 2H), 7.74 (dd, J = 6.4, 3.4 Hz, 2H), 7.44 (d, J = 8.1 Hz, 4H), 7.15 (d, J = 7.9 Hz, 4H), 2.37 (s, 6H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 153.7, 141.4, 138.9, 136.6, 129.9, 129.8, 129.3, 129.1, 21.5. HRMS (ESI-ion trap) m/z: $[M + H]^+$ calcd for $C_{22}H_{19}N_2$, 311.1548; found, 311.1548.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.9b01667.

X-ray crystal characterization data for compound **2a** (CIF)

$H_2{}^{18}O$ Isotopic labeling experiment and copies of ^{1}H, $^{13}C\{^1H\}$, ^{19}F NMR spectra (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: yangdq@scnu.edu.cn. Phone: +86 20 31040403. Fax: +86 20 31040403.

ORCID

Yu Chen: 0000-0002-4696-9269

Dingqiao Yang: 0000-0002-5226-7722

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We gratefully thank the National Natural Science Foundation of China (21172081, 21372090), the Natural Science Foundation of Guangdong Province (S2013020013091) and the City of Guangzhou Science and Technology Plan Projects (201510010054) for financial support.

■ REFERENCES

(1) For selected examples, see: (a) Rozwadowska, M. D.; Chrzanowska, M. Synthetic Entry into the Secoisoquinoline Alkaloids. *Tetrahedron* **1985**, *41*, 2885−2890. (b) Ngadjui, B. T.; Kouam, S. F.; Dongo, E.; Kapche, G. W. F.; Abegaz, B. M. Prenylated Flavonoids from the Aerial Parts of Dorstenia Mannii. *Phytochemistry* **2000**, *55*, 915−919. (c) Mahabusarakam, W.; Deachathai, S.; Phongpaichit, S.; Jansakul, C.; Taylor, W. C. A Benzil and Isoflavone Derivatives from Derris Scandens Benth. *Phytochemistry* **2004**, *65*, 1185−1191. (d) Nicolaou, K. C.; Gray, D. L. F.; Tae, J. Total Synthesis of Hamigerans and Analogues Thereof. Photochemical Generation and Diels−Alder Trapping of Hydroxy-o-quinodimethanes. *J. Am. Chem. Soc.* **2004**, *126*, 613−627. (e) Wadkins, R. M.; Hyatt, J. L.; Wei, X.; Yoon, K. J. P.; Wierdl, M.; Edwards, C. C.; Morton, C. L.; Obenauer, J. C.; Damodaran, K.; Beroza, P.; Danks, M. K.; Potter, P. M. Identification and Characterization of Novel Benzil (Diphenylethane-1,2-dione) Analogues as Inhibitors of Mammalian Carboxylesterases. *J. Med. Chem.* **2005**, *48*, 2906−2915.

(2) For selected examples, see: (a) Wolkenberg, S. E.; Wisnoski, D. D.; Leister, W. H.; Wang, Y.; Zhao, Z.; Lindsley, C. W. Efficient Synthesis of Imidazoles from Aldehydes and 1,2-Diketones Using Microwave Irradiation. *Org. Lett.* **2004**, *6*, 1453−1456. (b) Shipe, W. D.; Yang, F.; Zhao, Z.; Wolkenberg, S. E.; Nolt, M. B.; Lindsley, C. W. Convenient and General Microwave-Assisted Protocols for the Expedient Synthesis of Heterocycle. *Heterocycles* **2006**, *70*, 655−689. (c) Ghosh, P.; Mandal, A.; Subba, R. γ-Maghemite-silica nanocomposite: A green catalyst for diverse aromatic N-heterocycles. *Catal. Commun.* **2013**, *41*, 146−152. (d) Huang, T.-Q.; Qu, W.-Y.; Ding, J.-C.; Liu, M.-C.; Wu, H.-Y.; Chen, J.-X. Catalyst-Free Protocol for the Synthesis of Quinoxalines and Pyrazines in PEG. *Heterocycl. Chem.* **2013**, *50*, 293−297. (e) Ganji, P.; van Leeuwen, P. W. N. M. Phosphine Supported Ruthenium Nanoparticle Catalyzed Synthesis of Substituted Pyrazines and Imidazoles from α-Diketones. *J. Org. Chem.* **2017**, *82*, 1768−1774. (f) Tamaddon, F.; Tafti, A.; Pooramini, F. An Improved Synthesis of Multi-Substituted Pyrazines under Catalyst- and Solvent-Free Conditions. *Synthesis* **2016**, *48*, 4295−4299.

(3) Hernández-Cruz, O.; Zolotukhin, M. G.; Fomine, S.; Alexandrova, L.; Aguilar-Lugo, C.; Ruiz-Treviño, F. A.; Ramos-Ortíz, G.; Maldonado, J. L.; Cadenas-Pliego, G. High-Tg Functional Aromatic Polymers. *Macromolecules* **2015**, *48*, 1026−1037.

(4) (a) Song, L.-C.; Liu, P.-C.; Han, C.; Hu, Q.-M. Synthesis and Characterization of Cp_2Ti-Containing Organometallics *via* in Situ Oxidative-Addition of "Cp_2Ti" Intermediate.: Crystal Structures of $(1\text{-}C_{10}H_7S)_2TiCp_2$,$[(\eta_5\text{-}C_5H_5)Fe\ (\eta_5\text{-}C_5H_4CH_2S)]_2TiCp_2$ and $[\eta^2\text{-}OC(Ph)C(Ph)O]TiCp_2$. *J. Organomet. Chem.* **2002**, *648*, 119−125. (b) Spikes, G. H.; Sproules, S.; Bill, E.; Weyhermüller, T.; Wieghardt, K. One-and Two-Electron Reduced 1,2-Diketone Ligands in $[CrIII(L\bullet)_3](S= 0)$ and $Na_2(Et_2O)_2[VIV(LRed)_3](S=1/2)$. *Inorg. Chem.* **2008**, *47*, 10935−10944.

(5) (a) Dechert-Schmitt, A.-M.; Garnsey, M. R.; Wisniewska, H. M.; Murray, J. I.; Lee, T.; Kung, D. W.; Sach, N.; Blackmond, D. G. Highly Modular Synthesis of 1,2-Diketones via Multicomponent Coupling Reactions of Isocyanides as CO Equivalents. *ACS Catal.* **2019**, *9*, 4508−4515. (b) Ren, W.; Xia, Y.; Ji, S.-J.; Zhang, Y.; Wan, X.; Zhao, J. Wacker-Type Oxidation of Alkynes into 1,2-Diketones Using Molecular Oxygen. *Org. Lett.* **2009**, *11*, 1841−1844. (c) Byun, S.; Chung, J.; Lim, T.; Kwon, J.; Kim, B. M. Synthesis of Benzil Derivatives *via* Oxidation of Alkynes Catalyzed by Pd−Fe_3O_4 Heterodimer Nanocrystals. *RSC Adv.* **2014**, *4*, 34084−34088. (d) Wang, A.; Jiang, H.; Li, X. Palladium-Catalyzed Carbonation-Diketonization of Terminal Aromatic Alkenes via Carbon-Nitrogen Bond Cleavage for the Synthesis of 1,2-Diketones. *J. Org. Chem.* **2011**, *76*, 6958−6961. (e) Min, H.; Palani, T.; Park, K.; Hwang, J.; Lee, S. Copper-Catalyzed Direct Synthesis of Diaryl 1,2-Diketones from Aryl Iodides and Propiolic Acids. *J. Org. Chem.* **2014**, *79*, 6279−6285. (f) Su, Y.; Sun, X.; Wu, G.; Jiao, N. Catalyst-Controlled Highly Selective Coupling and Oxygenation of Olefins: A Direct Approach to Alcohols, Ketones, and Diketones. *Angew. Chem., Int. Ed.* **2013**, *52*, 9808−9812. (g) Giraud, A.; Provot, O.; Peyrat, J.-F.; Alami, M.; Brion, J.-D. Microwave-Assisted Efficient Synthesis of 1,2-Diaryldiketones: A Novel Oxidation Reaction of Diarylalkynes with DMSO Promoted by $FeBr_3$. *Tetrahedron* **2006**, *62*, 7667−7673. (h) Che, C.-M.; Yu, W.-Y.; Chan, P.-M.; Cheng, W.-C.; Peng, S.-M.; Lau, K.-C.; Li, W.-K. Alkyne Oxidations by *Cis*-Dioxoruthenium (VI) Complexes. A Formal [3+2] Cycloaddition Reaction of Alkynes with *cis*-$[(Cn^*)(CF_3CO_2)RuVIO_2]ClO_4$ (Cn^*= 1,4,7-trimethyl-1,4,7-triazacyclononane). *J. Am. Chem. Soc.* **2000**, *122*, 11380−11392. (i) Xu, C.-F.; Xu, M.; Jia, Y.-X.; Li, C.-Y. Gold-Catalyzed Synthesis of Benzil Derivatives and α-Keto Imides via Oxidation of Alkynes. *Org. Lett.* **2011**, *13*, 1556−1559. (j) Lv, W.-X.; Zeng, Y.-F.; Zhang, S.-S.; Li, Q.;

DOI: 10.1021/acs.joc.9b01667
J. Org. Chem. XXXX, XXX, XXX−XXX

Wang, H. Mild $Mn(OAc)_3$-Mediated Aerobic Oxidative Decarboxylative Coupling of Arylboronic Acids and Arylpropiolic Acids: Direct Access to Diaryl 1,2-Diketones. *Org. Lett.* **2015**, *17*, 2972−2975. (k) Shi, S.; Wang, T.; Yang, W.; Rudolph, M.; Hashmi, A. S. K. Gold-Catalyzed Synthesis of Glyoxals by Oxidation of Terminal Alkynes: One-Pot Synthesis of Quinoxalines. *Chem.—Eur. J.* **2013**, *19*, 6576−6580. (l) Trosien, S.; Waldvogel, S. R. Synthesis of Highly Functionalized 9,10-Phenanthrenequinones by Oxidative Coupling Using $MoCl_5$. *Org. Lett.* **2012**, *14*, 2976−2979. (m) Rogatchov, V. O.; Filimonov, V. D.; Yusubov, M. A Novel Practical Reaction of Diarylalkynes with Sulfur Trioxide: Oxidation to 1,2-Diketones. *Synthesis* **2001**, 1001−1003. (n) Chu, J.-H.; Chen, Y.-J.; Wu, M.-J. Mild Oxidation of Diarylacetylenes to 1,2-Diketones Using Oxone in Trifluoroacetic Acid. *Synthesis* **2009**, 2155−2162. (o) Wan, Z.; Jones, C. D.; Mitchell, D.; Pu, J. Y.; Zhang, T. Y. Practical Method for Transforming Alkynes into α-Diketones. *J. Org. Chem.* **2006**, *71*, 826−828. (p) Gao, A.; Yang, F.; Li, J.; Wu, Y. Pd/Cu-Catalyzed Oxidation of Alkynes into 1,2-Diketones Using DMSO as the Oxidant. *Tetrahedron* **2012**, *68*, 4950−4954.

(6) (a) Tan, K. J.; Wille, U. Activation of Molecular Oxygen by *S*-Radicals: Experimental and Computational Studies on a Novel Oxidation of Alkynes to α-Diketones. *Chem. Commun.* **2008**, 6239−6241. (b) Zhu, X.; Li, P.; Shi, Q.; Wang, L. Thiyl radical catalyzed oxidation of diarylalkynes to α-diketones by molecular oxygen under visible-light irradiation. *Green Chem.* **2016**, *18*, 6373−6379. (c) Liu, X.; Cong, T.; Liu, P.; Sun, P. Synthesis of 1,2-Diketones *via* a Metal-Free, Visible-Light-Induced Aerobic Photooxidation of Alkynes. *J. Org. Chem.* **2016**, *81*, 7256−7261.

(7) Mckillop, A.; Oldenziel, O. H.; Swann, B. P.; Taylor, E. C.; Robey, R. L. Thallium in organic synthesis. XXXIV. Oxidations of acetylenes with thallium(III) nitrate (TTN). *J. Am. Chem. Soc.* **1973**, *95*, 1296−1301.

(8) Jung, M. E.; Deng, G. Synthesis of α-Diketones from Alkylaryl- and Diarylalkynes Using Mercuric Salts. *Org. Lett.* **2014**, *16*, 2142−2145.

(9) Hering, T.; Slanina, T.; Hancock, A.; Wille, U.; König, B. Visible Light Photooxidation of Nitrate: The Dawn of a Nocturnal Radical. *Chem. Commun.* **2015**, *51*, 6568−6571.

(10) Ruengsangtongkul, S.; Chaisan, N.; Thongsornkleeb, C.; Tummatorn, J.; Ruchirawat, S. Rate Enhancement in CAN-Promoted $Pd(PPh_3)_2Cl_2$-Catalyzed Oxidative Cyclization: Synthesis of 2-Ketofuran-4-Carboxylate Esters. *Org. Lett.* **2019**, *21*, 2514−2517.

(11) (a) Niu, M.; Fu, H.; Jiang, Y.-Y.; Zhao, Y.-F. A Convenient and Practical Approach to α-Diketones via Reactions of Internal Aryl Alkynes with *N*-iodosuccinimide/Water. *Synthesis* **2008**, 2879−2882. (b) Ren, W.; Liu, J.; Chen, L.; Wan, X. Ruthenium-Catalyzed Alkyne Oxidation with Part-Per-Million Catalyst Loadings. *Adv. Synth. Catal.* **2010**, *352*, 1424−1428. (c) Xia, X.-F.; Gu, Z.; Liu, W.; Wang, N.; Wang, H.; Xia, Y.; Gao, H.; Liu, X. Selective Oxygenation of Alkynes: A Direct Approach to Diketones and Vinyl Acetate. *Org. Biomol. Chem.* **2014**, *12*, 9909−9913. (d) Chikugo, T.; Yauchi, Y.; Ide, M.; Iwasawa, T. Transition Metal-Free Oxidation of Ynamides for Synthesis of α-Keto-Imides. *Tetrahedron* **2014**, *70*, 3988−3993. (e) Kim, S. W.; Um, T.-W.; Shin, S. Metal-Free Iodine-Catalyzed Oxidation of Ynamides and Diaryl Acetylenes into 1,2-Diketo Compounds. *J. Org. Chem.* **2018**, *83*, 4703−4711.

(12) Yang, W.; Yao, Y.; Yang, X.; Deng, Y.; Lin, Q.; Yang, D. Synthesis of C4-Alkynylisoxazoles *via* a Pd-Catalyzed Sonogashira Cross-Coupling Reaction. *RSC Adv.* **2019**, *9*, 8894−8904.

(13) CCDC 1864229 (**2a**) Contains He Supplementary Crystallographic Data for This Paper. These Data Can be Obtained Free of Charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(14) Zhang, C.; Zong, X.; Zhang, L.; Jiao, N. Copper-Catalyzed Aerobic Oxidative Cross-Dehydrogenative Coupling of Amine and α-Carbonyl Aldehyde: A Practical and Efficient Approach to α-Ketoamides with Wide Substrate Scope. *Org. Lett.* **2012**, *14*, 3280−3283.

(15) (a) Chambrs, R. M.; Heard, A. C.; Wayne, R. P. Inorganic Gas-Phase Reactions of the Nitrate Radical: $I_2 + NO_3$ and $I + NO_3$. *J. Phys. Chem.* **1992**, *96*, 3321−3331. (b) Chikugo, T.; Yauchi, Y.; Ide, M.; Iwasawa, T. Transition metal-free oxidation of ynamides for synthesis of α-keto-imides. *Tetrahedron* **2014**, *70*, 3988−3993. (c) Jiang, S.; Li, Y.; Luo, X.; Huang, G.; Shao, Y.; Li, D.; Li, B. $NH_4I/EtOCS_2K$ Promoted Synthesis of Substituted Benzils from Diphenylacetylene Derivatives. *Tetrahedron Lett.* **2018**, *59*, 3249−3252. (d) Katrun, P.; Mueangkaew, C.; Pohmakotr, M.; Reutrakul, V.; Jaipetch, T.; Soorukram, D.; Kuhakarn, C. Regioselective C2 Sulfonylation of Indoles Mediated by Molecular Iodine. *J. Org. Chem.* **2014**, *79*, 1778−1785. (e) Zhang, J.; Liang, Z.; Wang, J.; Guo, Z.; Liu, C.; Xie, M. Metal-Free Synthesis of Functionalized Tetrasubstituted Alkenes by Three-Component Reaction of Alkynes, Iodine, and Sodium Sulfinates. *ACS Omega* **2018**, *3*, 18002−18015.

(16) Feng, C.; Loh, T.-P. Palladium-Catalyzed Decarboxylative Cross-Coupling of Alkynyl Carboxylic Acids with Arylboronic Acids. *Chem. Commun.* **2010**, *46*, 4779−4781.

(17) Ojha, D. P.; Prabhu, K. R. Regioselective Synthesis of Vinyl Halides, Vinyl Sulfones, and Alkynes: A Tandem Intermolecular Nucleophilic and Electrophilic Vinylation of Tosylhydrazones. *Org. Lett.* **2015**, *17*, 18−21.

(18) Shi, L.; Jia, W.; Li, X.; Jiao, N. Cu-Catalyzed Decarboxylative Coupling of Propiolic Acids with Boronic Acids. *Tetrahedron Lett.* **2013**, *54*, 1951−1955.

(19) Lin, C.-H.; Wang, Y.-J.; Lee, C. F. Efficient Copper-Catalyzed Cross-Coupling Reaction of Alkynes with Aryl Iodides. *Eur. J. Org. Chem.* **2010**, 4368−4371.

(20) Sagadevan, A.; Hwang, K. C. Photo-Induced Sonogashira C−C Coupling Reaction Catalyzed by Simple Copper(I) Chloride Salt at Room Temperature. *Adv. Synth. Catal.* **2012**, *354*, 3421−3427.

(21) Zhou, T.; Yu, X.; Feng, X.; Bao, M. An Efficient Transformation of Primary Halides into Nitriles Through Palladium-Catalyzed Hydrogen Transfer Reaction. *Chem. Commun.* **2015**, *51*, 10714−10717.

(22) Yan, H.; Wang, H.; Li, X.; Xin, X.; Wang, C.; Wan, B. Rhodium-Catalyzed C−H Annulation of Nitrones with Alkynes: A Regiospecific Route to Unsymmetrical 2,3-Diaryl-Substituted Indoles. *Angew. Chem., Int. Ed.* **2015**, *54*, 10613−10617.

(23) Mao, J.; Xie, G.; Wu, M.; Guo, J.; Ji, S. Ligand-Free Iron/Copper Cocatalyzed Alkynylation Coupling Reactions. *Adv. Synth. Catal.* **2008**, *350*, 2477−2482.

(24) Hu, H.; Yang, F.; Wu, Y. Palladacycle-Catalyzed Deacetonative Sonogashira Coupling of Aryl Propargyl Alcohols with Aryl Chlorides. *J. Org. Chem.* **2013**, *78*, 10506−10511.

DOI: 10.1021/acs.joc.9b01667
J. Org. Chem. XXXX, XXX, XXX−XXX