JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

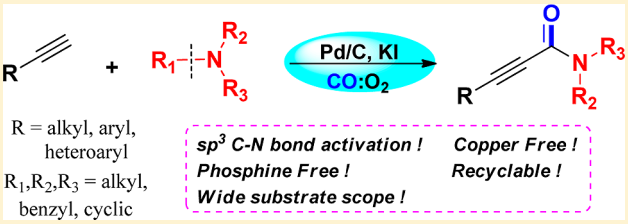
Palladium-Catalyzed Oxidative *N*-Dealkylation/Carbonylation of Tertiary Amines with Alkynes to α,β-Alkynylamides

Rajendra S. Mane and Bhalchandra M. Bhanage*

Department of Chemistry, Institute of Chemical Technology, Mumbai 400019, India

Supporting Information

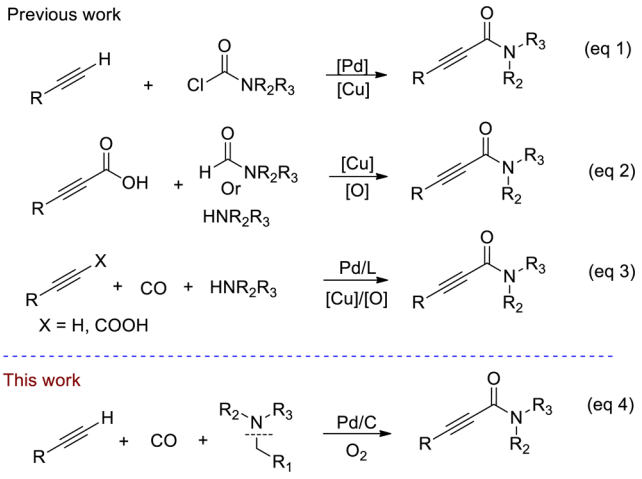
ABSTRACT: The first highly effective Pd/C-catalyzed oxidative *N*-dealkylation/carbonylation of various aliphatic as well as cyclic tertiary amines with alkynes has been described. The selective sp^3 C−N bond activation of tertiary amines at the less steric side using O_2 as a sole oxidant and a plausible reaction pathway for the reaction are discussed. The general and operationally simple methodology provides an alternative for the synthesis of a wide range of alk-2-ynamide derivatives under mild conditions. The present protocol is ecofriendly and practical, and it shows significant recyclability.



INTRODUCTION

Alk-2-ynamide (α,β-alkynylamide) derivatives are important building blocks in organic synthesis and often fundamental scaffolds of pharmaceutically relevant compounds.[1] This class of compounds plays a crucial role in natural products as well as key intermediates in the synthesis of heterocycles.[2] Historically, tertiary amides have been synthesized by Pd/Cu-catalyzed cross-coupling reaction of alkynes with carbamoyl chlorides (Scheme 1, eq 1).[3] Moreover, Cu/TBHP-mediated synthesis of tertiary amides can be achieved by using propiolic acids and its derivatives treated with secondary amines[4] or formamides[5] (Scheme 1, eq 2). Some drawbacks exist; nevertheless, these methodologies suffer from multistep synthesis and limited stability of carbamoyl chlorides, i.e., moisture sensitivity and lack of functional group tolerance with severe conditions.

Scheme 1. Synthetic Approach for the Synthesis of Alkynylamides



Over the past decade, transition-metal-catalyzed carbonylation reactions have gained great prominence in organic chemistry.[6] Carbon monoxide is a C1 building block in organic synthesis and is valued because of its simplicity and atom economy.[7] Palladium-catalyzed oxidative carbonylation reactions of alkynes with amines represents the most straightforward approach to generate alkynylamides (Scheme 1, eq 3). The oxidative carbonylation between two nucleophiles is a very challenging task.[8] A literature survey reveals that there are few reports known for the oxidative carbonylation of alkynes or propiolic acid using primary/secondary amines.[9] Hoberg et al. reported Ni(II)-catalyzed carbonylative synthesis of alkynylamides by treating with alkynes using secondary amines as amine source.[9a,b] Furthermore, Gabriele et al. first reported the PdI_2/KI-catalyzed oxidative carbonylation for the synthesis of alkynylamides from alkynes and secondary amines in the presence of a CO/air mixture (20 atm) for 24 h.[9c] The Yamamoto group employed $PdCl_2/PPh_3$ as a catalytic system for the direct oxidative aminocarbonylation using $CO/O_2$with 2 equiv of AcONa as base.[9d] Our group also disclosed Pd/C and TBAI as a catalytic system, and the Xia group employed Pd-NHC/K_3PO_4 (2 equiv) for the synthesis of alkynylamides using secondary amines as an aminal source.[9e,f] Lee and Wu et al. also reported $Pd(OAc)_2$/AgO (1 equiv) and $Pd_2(dba)_3$/Xphos/$Co_2(CO)_8$ as a carbonyl source mediated synthesis of alkynylamides through the carbonylation of propiolic acids with primary/secondary amines.[9g,h] Although their catalytic activities are excellent, the development of a more efficient, selective, and general method for the direct synthesis of alkynylamides is thus highly desirable. The development of heterogeneous, recyclable, cost-efficient, and environmentally benign protocols to reduce the high production costs as well as

Received: February 23, 2016
Published: May 16, 2016

DOI: 10.1021/acs.joc.6b00386
J. Org. Chem. 2016, 81, 4974−4980

possible heavy-metal contamination remains essential. Nevertheless, these reported methodologies typically suffer from harsh conditions, requirement of stoichiometric copper as a co-catalyst or oxidant, excess base to inhibit the undesired homocoupling of alkynes, and limited substrate scope with tedious workup. To circumvent these problems, we envisioned tertiary amines as an aminal source, which slowly releases in situ secondary amines through the oxidative *N*-dealkylation/carbonylation of tertiary amines with alkynes, which in turn could easily lead us to direct synthesis of alkynylamides (Scheme 1, eq 4). However, the oxidative *N*-dealkylation/carbonylation of tertiary amines with alkynes using Pd/C with O_2 remains elusive because of several fundamental challenges such as homocoupling of alkynes, tandem annulations, and urea formation. Hence, these challenges need to be overcome.

In recent years, the C−N bond activation of highly stable tertiary amines has emerged as an important approach in synthetic chemistry.[10,11] In this context, among the various known amine surrogates that could be used as nucleophile, tertiary amines stand out as particularly attractive substrates in terms of their availability. To the best of our knowledge, the use of stable tertiary amines as an aminal source for this transformation is unprecedented. Very recently, we demonstrated oxidative C−N bond activation of inert tertiary amines to tertiary amides via aminocarbonylation of aryl iodides.[12] Based on our research interest in oxidative carbonylation reactions,[13] herein we report the first phosphine-free Pd/C-catalyzed oxidative *N*-dealkylation/carbonylation of aliphatic as well as cyclic tertiary amines with terminal alkynes.

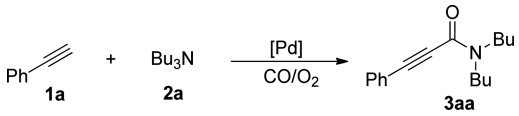
RESULTS AND DISCUSSION

We began the alk-2-ynamide synthesis using phenylacetylene (**1a**) and Bu_3N (**2a**) as model substrates. The reaction was performed in MeCN, using 5 mol % of $PdCl_2(PPh_3)_2$ as a catalyst and 3 mmol of K_3PO_4 as a base under CO/O_2 pressure at 100 °C for 24 h. The alkynylamide product **3aa** was only obtained in <5% yield. The iodide additive had a significant impact on the reaction efficiency. Surprisingly, when TBAI was used as an additive, the overall yield of the desired product increased to 68% (Table 1, entry 2). Subsequently, the evaluation of additives revealed that KI was the best and afforded 86% yield of **3aa** (Table 1, entry 4). Next, various palladium precursors including heterogeneous sources were screened as shown in Table 1. Interestingly, 10% Pd/C was found to be the most effective catalyst for this transformation and furnished an excellent yield of **3aa** in the absence of base (Table 1, entry 11). The use of 3 mol % of Pd/C was found to be adequate for this reaction. Next, we studied the effect of amount of KI, and it was observed that 0.1 mmol of KI provides the highest yield of **3aa** (Table 1, entry 12).

In the next set of experiments, the effects of solvents such as acetonitrile, 1,4-dioxane, THF, and toluene were examined. Among these, acetonitrile was the best solvent and provided a 94% yield of **3aa** (Table 2, entry 1). Remarkably, under CO/O_2 (5:1) pressure, the alkynylamide product **3aa** was obtained with a yield of 94% (Table 2, entry 6).[9] Notably, when air was used as oxidant instead of O_2, the yield of **3aa** decreased significantly, and no formation of product was noted when the reaction was performed under inert atmosphere (Table 2, entries 8 and 9). This suggests that the additives are crucial in this transformation with molecular oxygen as sole oxidant. A decrease in the reaction temperature to 70 °C led to a decrease in the yield of **3aa**, while an increase had no significant effect on the yield (Table 2, entries 10−12).

To demonstrate the general applicability of this new catalytic system, initially the *N*-dealkylation/carbonylation of various tertiary amines with **1a** was examined under the optimized reaction conditions. As shown in Table 3, this transformation proceeded quite smoothly and afforded the desired alkynylamides in a good to excellent yields. Both symmetrical as well as unsymmetrical tertiary amines could be well tolerated (**3aa**−

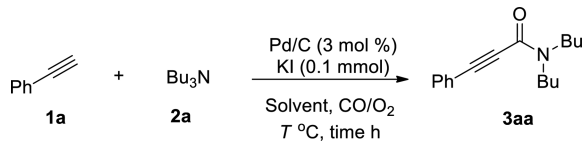
Table 1. Effect of Additive, Catalyst, and Catalyst Loading[a]



entry	catalyst	base	additive	yield[b] (%)
1[c]	$PdCl_2(PPh_3)_2$	K_3PO_4		<5
2	$PdCl_2(PPh_3)_2$	K_3PO_4	TBAI	68
3	$PdCl_2(PPh_3)_2$	K_3PO_4	TBAB	59
4	$PdCl_2(PPh_3)_2$	K_3PO_4	KI	86
5	$PdCl_2(PPh_3)_2$	K_3PO_4	NaI	79
6	$PdCl_2$	K_3PO_4	KI	91
7	$PdBr_2$	K_3PO_4	KI	63
8	$Pd(OAc)_2$	K_3PO_4	KI	81
9	10% Pd/C	K_3PO_4	KI	92
10	5% Pd/C	K_3PO_4	KI	84
11	10% Pd/C		KI	95
12[d]	10% Pd/C		KI	94
13[e]	10% Pd/C		KI	94
14[f]	10% Pd/C		KI	87

[a]Reaction conditions: **1a** (1 mmol), **2a** (1.5 mmol), Pd (5 mol %), K_3PO_4 (3 mmol), additive (0.5 mmol), CO/O_2 = 9/1 in 10 mL of MeCN, 100 °C, 8 h. [b]Yields were determined by GC. [c]24 h. [d]0.1 mmol of KI was used. [e]3 mol % of Pd/C was used. [f]2 mol % of Pd/C was used.

Table 2. Optimization of Reaction Parameters[a]

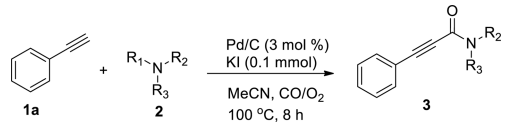


entry	solvent	CO/O_2 (atm)	T (°C)	time (h)	yield[b] (%)
1	MeCN	9:1	100	8	94
2	1,4-dioxane	9:1	100	8	52
3	THF	9:1	100	8	67
4	Toluene	9:1	100	8	74
5	MeCN	7:1	100	8	95
6	MeCN	5:1	100	8	94
7	MeCN	3:1	100	8	92
8[c]	MeCN	5:1	100	8	69
9	MeCN	5:0	100	8	NR
10	MeCN	5:1	120	8	89
11	MeCN	5:1	80	8	81
12	MeCN	5:1	70	8	53
13	MeCN	5:1	100	12	94
14	MeCN	5:1	100	5	86
15	MeCN	5:1	100	4	77

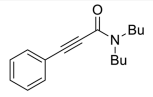
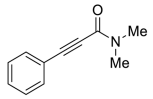
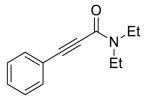
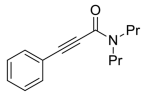
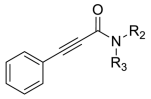
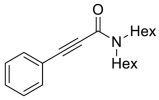
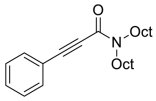
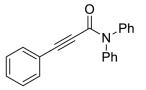
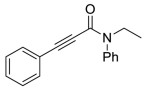
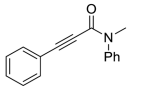
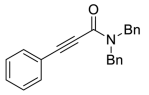
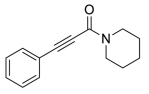
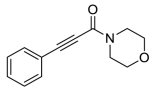
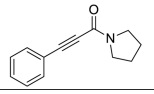
[a]Reaction conditions: **1a** (1 mmol), **2a** (1.5 mmol), 10% Pd/C (3 mol %), KI (0.1 mmol), CO/O_2 = 5/1 in 10 mL of MeCN, 100 °C, 8 h. [b]GC yield. [c]1 atm of air. NR = no reaction.

DOI: 10.1021/acs.joc.6b00386
J. Org. Chem. 2016, 81, 4974−4980

Table 3. Scope of Carbonylation of 1a with Tertiary Amine as Amine Source[a]



1a + 2 → 3

entry	amine	product		yield (%)[b]
1	Bu_3N		**3aa**	94, 82[c]
2	Me_3N		**3ab**	83
3	Me_2Noct		**3ab**	87
4	Et_3N		**3ac**	88
5	Pr_3N		**3ad**	92
6	*i*-Pr_2EtN		**3aea** R_2, R_3 = *i*-Pr **3aeb** R_2 = Et, R_3 = *i*-Pr	49 32
7	Hex_3N		**3af**	93
8	Oct_3N		**3ag**	85
9	Ph_3N		**3ah**	NR
10	$PhNEt_2$		**3ai**	NR
11	$PhNMe_2$		**3aj**	NR
12	Bn_3N		**3ak**	NR
13			**3al**	38
14			**3al**	32
15			**3am**	34
16			**3am**	29
17			**3an**	45

[a]Reaction conditions: **1a** (1 mmol), **2** (1.5 mmol), 10% Pd/C (3 mol %), KI (0.1 mmol), CO/O_2 = 5/1 in 10 mL of MeCN, 100 °C, 8 h. [b]Isolated yield. [c]With 5.0 mmol of **1a**.

an). For symmetrical tertiary amines, the selectivity of the *N*-dealkylation was found to be independent of the alkyl chain lengths, and oxidative *N*-dealkylation/carbonylation of different aliphatic amines with **1a** afforded the corresponding amides in high yields. When *N*,*N*-diisopropylethylamine was employed, potentially two kinds of *N*-dealkylation were observed. This resulted into formation of two types of products (**3aea** and **3aeb**). Gratifyingly, *N*,*N*-dimethyloctylamine was also efficiently utilized in this transformation, and selective cleavage of C−N bond at the longest chain was observed (**3ab**).

Surprisingly, no products were observed with Ph_3N, $PhNEt_2$, and $PhNMe_2$ as the tertiary amine source, which could be because of the lack of hydrogen atoms α to the nitrogen and because the lone pair of nitrogen is conjugated with the phenyl ring, thus suggesting that the sp^2 C−N bond does not cleave under these conditions (Table 3, entries 9−11). When Bn_3N was employed, the reaction did not also proceed, which could be because of the steric hindrance of benzyl group (Table 3, entry 12). To our delight, cyclic tertiary amines, i.e., *N*-ethyl- or *N*-methyl-substituted, afforded **3al**, **3am**, and **3an**, respectively. These results indicate that a sterically less hindered alkyl group was more facile for this transformation.

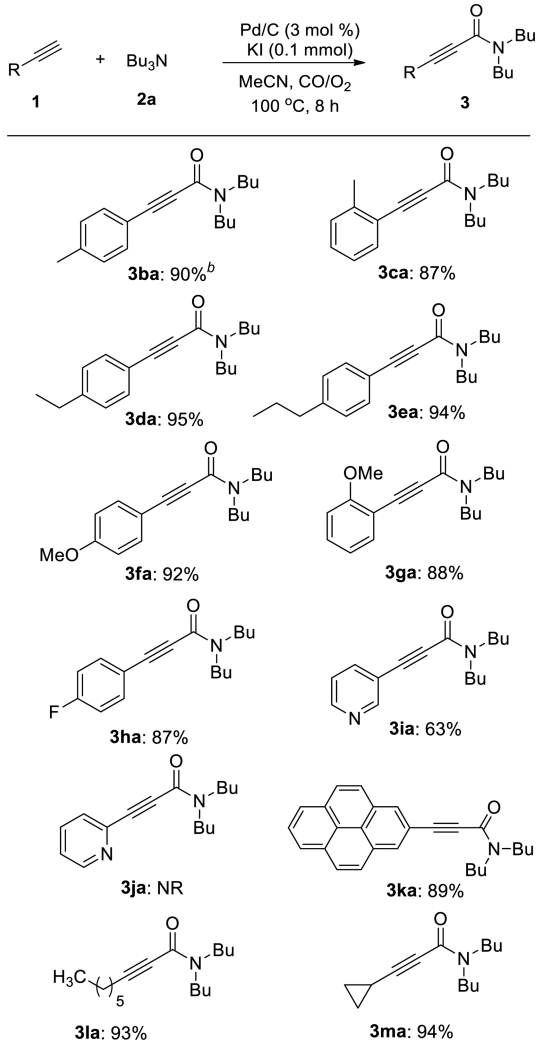
We next investigated the scope of aromatic alkynes **1** with *N*-dealkylation of Bu_3N **2a** under the optimal conditions, and the results are shown in Scheme 2. Both electron-donating and electron-deficient substituents on the phenyl ring of alkynes were well tolerated and afforded excellent yields (**3ba**−**ha**). Remarkably, the reaction with heteroaromatic alkyne **1i** (3-ethynylpyridine) furnished the corresponding product (**3ia**). However, alkyne **1j** (2-ethynylpyridine) did not undergo the transformation, possibly due to the formation of a chelate with the nitrogen atom of the pyridine ring and the alkyne. It is worth noting that aliphatic alkynes were also found to be compatible with this protocol, thus providing **3la** and **3ma** in high yield. Interestingly, the reaction with highly conjugated 2-ethynylpyrene also gave an excellent yield of **3ka**. It is worth mentioning that pyrene and its derivatives show fluorescence, having potential applications in OLEDs as efficient emitters.[14]

To gain insight into the role of additives in the reaction mechanism, several control experiments were carried out (Scheme 3). First, when Bu_3N **2a** as amine source was subjected to the optimized conditions, the alkynylamide product was obtained in an excellent yield (**3aa**, 96% yield), while in the absence of additive the reaction failed to generate carbonylated product **3aa**, indicating that additives are crucial in this transformation. To our delight, when we used Bu_2NH as the amine source, only 57% of **3aa** was obtained with tetrabutylurea as by product. These results indicate that the tertiary amine slowly releases in situ secondary amine under the optimized reaction conditions, which in turn could provide the highest yield of **3aa**.

From the green and sustainable chemistry point of view, the recyclability of Pd/C catalyst was investigated. After the first reaction cycle, the catalyst was recovered from the reaction mixture and washed with an excess of solvent and then finally with methanol to remove trace amounts of product. After washing and drying, recovered catalyst could be reused up to six times with a slight decrease in catalytic activity (95% to 89%). In order to check the leaching of palladium metal, first and sixth recycled samples were subjected to the inductively coupled plasma atomic emission spectrometry (ICP-AES) technique. No detectable amounts of palladium (below 0.1 ppm) were found, indicating a negligible catalyst leaching.

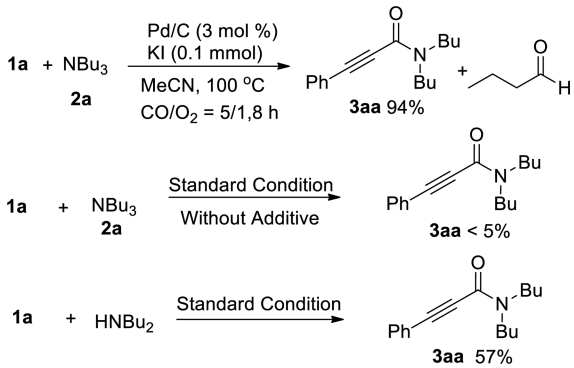
DOI: 10.1021/acs.joc.6b00386
J. Org. Chem. 2016, 81, 4974−4980

Scheme 2. Scope of Carbonylation of Various Terminal Alkynes with 2a[a]



[a]Reaction conditions: **1** (1 mmol), **2a** (1.5 mmol), 10% Pd/C (3 mol %), KI (0.1 mmol), CO/O_2 = 5/1 in 10 mL of MeCN, 100 °C, 8 h. [b]Isolated yield.

Scheme 3. Some Control Experiments



On the basis of the results obtained and previous reports, we propose two plausible reaction pathways for the *N*-dealkylation of tertiary amine to secondary amine as shown in Scheme 4.[10,11] In path A, the nitrogen of tertiary amine coordinates with Pd^0 to give the Pd-iminium type intermediate.[15b,d] Then, the iminium intermediate was hydrolyzed to provide secondary amine and aldehyde.[10g,h,12] At this stage, another possible pathway cannot be ruled out (path B).

In path B, the tertiary amine reacts with iodine to give an ammonium iodide.[16a,c] Subsequently, iminium iodide can be generated through the elimination of HI. Further, iminium iodide hydrolyzes to provide secondary amine and aldehyde. The mechanism for the oxidative carbonylation of alkynes with amines using Pd/C−KI is not clear at the moment; on the basis of the experimental results and previous reports, a plausible reaction pathway is outlined. Initially, in situ Pd(0) to Pd−I as an active species **I** could be generated in the presence of iodide promoter (KI) with O_2 as an terminal oxidant.[8h−j] As shown in Scheme 4, *N*-palladated **II** can be generated from amine and Pd−I. Then, the insertion of CO forms intermediate **III**, which can further react with alkyne to produce desired amide **3** and **IV**. The intermediate **IV** is reoxidized to Pd−I as an active catalytic species **I** in the presence of O_2, which completes the catalytic cycle.

In summary, we have illustrated a highly efficient strategy for the oxidative *N*-dealkylation/carbonylation of inert tertiary amines with alkynes. This conversion has been accomplished by using O_2 as an ideal oxidant and is catalyzed by Pd/C. This is the first instance where an extensive synthesis of alkynylamides via sp^3 C−N bond activation of various tertiary amines as an aminal source has been achieved. It is striking that substrates including heteroaryl as well as aliphatic alkynes were also compatible. Additionally, this approach has numerous advantageous such as being recyclable, phosphine free, cocatalyst free, and base free, and it uses molecular oxygen as an ideal and greener oxidant.

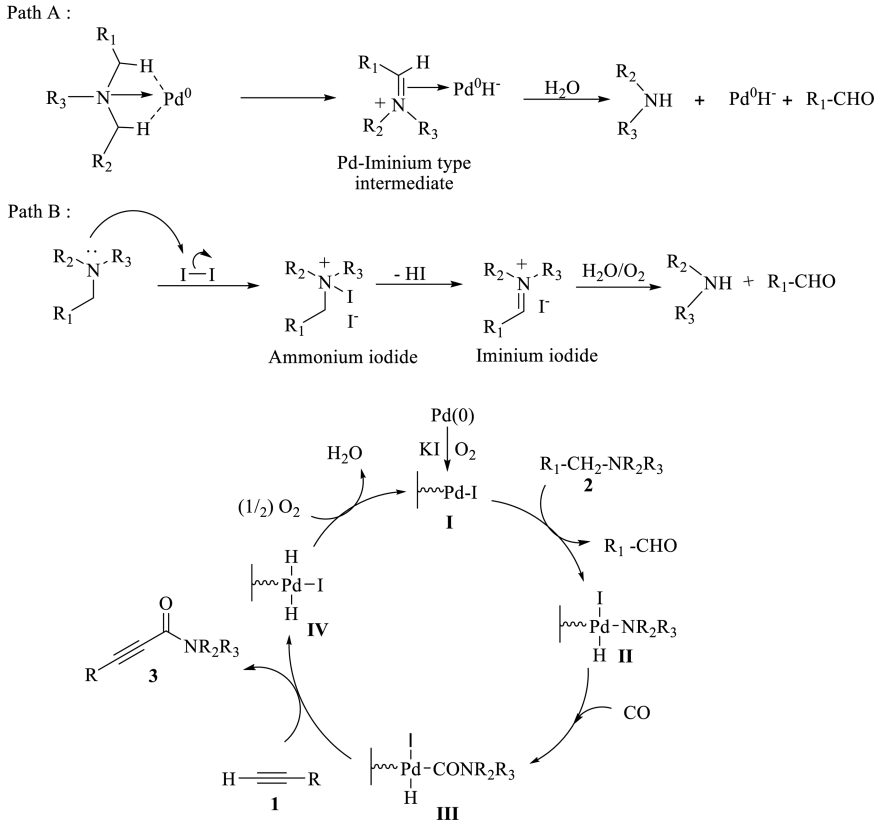
EXPERIMENTAL SECTION

General Methods. Pd/C was purchased from Sigma-Aldrich (10 wt % loading, matrix: activated carbon support, product no. 205699). Solvents were purchased with high purity and used without purification. All of the reactions were monitored by using TLC, GC, and GC−MS techniques. Products were purified by column chromatography on silica (100−200 mesh). The ^1H NMR spectrum was recorded on 400 and 500 MHz spectrometers in $CDCl_3$ using tetramethylsilane (TMS) as internal standard. The ^{13}C NMR spectrum was recorded on 100 and 125 MHz spectrometers in $CDCl_3$. Chemical shifts are reported in parts per million (δ) relative to tetramethylsilane as internal standard. The *J* (coupling constant) values are described in hertz. Splitting patterns of proton are depicted as s (singlet), d (doublet), t (triplet), and m (multiplet). HRMS (ESI) were taken on Orbitrap (quadrupole plus ion trap) and TOF mass analyzers. The products were confirmed by the comparison of their GC−MS, LC−MS, ^1H and ^{13}C NMR, and high-resolution mass spectra (HR-MS).

General Experimental Procedure for Oxidative *N*-Dealkylation/Carbonylation of Tertiary Amines with Alkynes. To a 100 mL stainless steel reactor were added alkyne (1 mmol), tertiary amine (1.5 mmol), 10% Pd/C (3 mol %), and KI (0.1 mmol) in 10 mL of MeCN. Then autoclave was closed and pressurized with oxygen (1 atm) and CO (5 atm) without flushing. The reaction mixture was stirred with a mechanical stirrer (550 rpm) and heated at 100 °C for 8 h. The reactor was then cooled to room temperature and degassed carefully, and the reactor was opened. The reactor vessel was washed with ethyl acetate (3 × 5 mL) to remove traces of product and catalyst if present. The reaction mixture was filtered, filtrates were washed with a saturated solution of sodium thiosulfate (3 × 5 mL) and dried over Na_2SO_4, and the solvent was evaporated under vacuum. Products were purified using column chromatography (silica gel 100−200 mesh, petroleum ether/ethyl acetate) to afford the corresponding products in good to excellent yield. The purity of compounds was confirmed by LCMS and GCMS analysis. The structure of products was confirmed

DOI: 10.1021/acs.joc.6b00386
J. Org. Chem. 2016, 81, 4974−4980

Scheme 4. Plausible Reaction Mechanism



by LCMS, GCMS, HRMS, ^{1}H NMR, and ^{13}C NMR spectroscopic techniques. (*Caution! CO and O_2 may form an explosive mixture under certain conditions.*)

Procedure for Recycling of Catalyst. After completion of the reaction, the recovered catalyst was washed with distilled water (3 × 5 mL) and finally with methanol (3 × 5 mL) to remove trace amounts of organic material. The catalyst was then dried in an oven at 80 °C for 5 h. After washing and drying, the recovered catalyst was found to be effectively recycled for up to six runs without any loss of catalytic activity and selectivity.

*N,N-Dibutyl-3-phenylpropiolamide (**3aa**).* Yellowish oil; 244.5 mg, 94% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (dd, J = 8.1, 1.4 Hz, 2H), 7.41−7.16 (m, 3H), 3.74−3.46 (m, 2H), 3.43−3.23 (m, 2H), 1.70−1.46 (m, 2H), 1.44−1.14 (m, 2H), 0.99−0.72 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.4, 132.2, 129.8, 128.4, 120.8, 89.2, 82.1, 48.9, 44.6, 31.0, 29.5, 20.2, 19.9, 13.8, 13.8.GC−MS (EI, 70 eV) m/z: 257 (2) $[M]^+$, 228 (3), 214(13), 173(4), 129 (100), 101(5), 75(6). HRMS (ESI) calcd for $[(C_{17}H_{23}NO)H]$ $[M + H]^+$: 258.1858, found 258.1856.

*N,N-Dimethyl-3-phenylpropiolamide (**3ab**).*[5b] White solid, mp 97−99 °C; 143.6 and 150.5 mg, 83 and 87% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ7.52−7.49 (m, 2H), 7.35 (dd, J = 14.9, 7.3 Hz, 3H), 3.25 (s, 3H), 2.99 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ154.6, 132.3, 129.9, 128.4, 120.6, 90.1, 81.5, 77.3, 77.0, 76.7, 38.3, 34.1. GC−MS (EI, 70 eV) m/z: 173 (55) $[M]^+$, 172 (4), 144 (9), 130 (12), 129 (100), 101 (11), 75 (17), 51 (7).

*N,N-Diethyl-3-phenylpropiolamide (**3ac**).*[5b,9f] Colorless oil; 176.9 mg, 88% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ7.52−7.49 (m, 2H), 7.38−7.24 (m, 3H), 3.64 (q, J = 7.1 Hz, 2H), 3.45 (q, J = 7.2 Hz, 2H), 1.27−1.23 (m, 3H), 1.17−1.13 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.9, 132.3, 129.8, 129.6, 128.9, 128.4, 120.7, 89.0, 81.9, 77.3, 77.0, 76.7, 43.6, 39.3, 14.4, 14.0, 12.8. GC−MS (EI, 70 eV) m/z: 201 (17.5) $[M]^+$, 200 (44), 186 (25), 130 (11.4), 129 (100), 101 (11), 75 (14.5), 51 (5).

*N,N-Dipropyl-3-phenylpropiolamide (**3ad**).*[9f,g] Colorless oil; 210.8 mg, 92% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ7.50 (t, J = 8.7 Hz, 2H), 7.44−7.34 (m, 3H), 3.57−3.54 (t, 2H), 3.37−3.34 (t, 2H), 1.71−1.57 (m, 4H), 0.93 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.5, 133.6, 132.2, 130.1, 128.4, 128.4, 120.8, 89.3, 82.1, 77.3, 76.9, 76.6, 50.8, 46.5, 22.2, 20.7, 11.3, 11.2. GC−MS (EI, 70 eV) m/z: 229 (4) $[M]^+$, 214 (6), 200 (23), 130 (11.5), 129 (100), 101 (6), 75 (6).

*N,N-Diisopropyl-3-phenylpropiolamide (**3aea**).*[5b] Yellowish oil; 112.2 mg, 49% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (dd, J = 8.0, 1.4 Hz, 2H), 7.38−7.28 (m, 3H), 4.64−4.52 (m, 1H), 3.75−3.62 (m, 1H), 1.34 (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.6, 132.1, 129.6, 128.4, 121.0, 88.5, 83.1, 50.3, 45.7, 29.6, 22.4, 21.0, 20.1. GC−MS (EI, 70 eV) m/z: 229 (5) $[M]^+$, 214 (8), 186 (11), 129 (100), 79 (15), 43 (5). HRMS (ESI) calcd for $[(C_{15}H_{19}NO)H]$ $[M + H]^+$: 230.1545, found 230.1539.

*N-Ethyl-N-isopropyl-3-phenylpropiolamide (**3aeb**).* Colorless oil; 68.5 mg, 32% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ7.58−7.43 (m, 2H), 7.36 (dd, J = 6.8 Hz, 3H), 4.82−4.55 (m, 1H), 3.55 (q, J = 7.1 Hz, 1H), 3.34 (q, J = 7.1 Hz, 1H), 1.35−1.16 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.9, 132.3, 132.2, 129.8, 128.4, 128.4, 120.8, 89.5, 81.9, 50.6, 39.3, 21.8, 20.4, 14.5. GC−MS (EI, 70 eV) m/z: 214 (18) $[M]^+$, 200 (11), 172 (3), 129 (100), 101 (6.5), 75 (3), 42 (4). HRMS (ESI) calcd for $[(C_{14}H_{17}NO)H]$ $[M + H]^+$: 216.1388, found 216.1383.

*N,N-Dihexyl-3-phenylpropiolamide (**3af**).* Yellowish oil; 291.1 mg, 93% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56−7.45 (m, 2H), 7.32 (m, 3H), 3.61−3.52 (m, 2H), 3.41−3.32 (m, 2H), 1.57 (m, 4H), 1.27 (m, 12H), 0.85−0.79 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.4, 132.2, 129.8, 128.4, 120.7, 89.4, 82.0, 49.2, 44.9, 34.0, 31.5, 31.4, 31.2, 28.8, 27.4, 26.6, 26.4, 24.4, 22.5, 22.3, 14.0, 13.9. GC−MS (EI, 70 eV) m/z: 313 (2) $[M]^+$, 312 (4), 284 (2), 256 (4), 242 (10), 200 (3.5), 172(6), 162 (10), 129 (100), 119 (10), 92 (7), 75 (3), 43(5). HRMS (ESI) calcd for $[(C_{21}H_{31}NO)H]$ $[M + H]^+$: 314.2484, found 314.2479.

*N,N-Dioctyl-3-phenylpropiolamide (**3ag**).* Colorless oil; 312.5 mg, 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (dd, J = 8.1, 1.4 Hz, 2H), 7.41−7.29 (m, 3H), 3.75−3.54 (m, 4H), 3.43−3.20 (m, 4H), 1.61 (s, 4H), 1.32−1.21 (m, 20H), 0.87−0.81 (m, 6H). ^{13}C NMR

DOI: 10.1021/acs.joc.6b00386
J. Org. Chem. 2016, 81, 4974−4980

(100 MHz, $CDCl_3$): δ 154.4, 132.2, 129.8, 128.4, 120.8, 89.2, 82.1, 49.1, 44.8, 31.7, 31.7, 29.3, 29.2, 29.2, 29.1, 28.9, 27.5, 27.0, 26.7, 22.6, 22.5, 14.0. GC−MS (EI, 70 eV) *m/z*: 368 (2) $[M]^+$, 355 (4), 326 (2.6), 298 (3.4), 270 (10), 172 (5), 129 (100), 115 (4), 77 (8), 57 (9), 44 (20), 32 (92). HRMS (ESI) calcd for $[(C_{25}H_{39}NO)H]$ $[M + H]^+$: 370.3110, found 370.3104.

3-Phenyl-1-(piperidin-1-yl)prop-2-yn-1-one (**3al**).[5b,9g] White solid, mp 79−81 °C; 80.9 and 68.1 mg, 38 and 32% yield. ^1H NMR (400 MHz, $CDCl_3$): δ7.53−7.51 (m, 2H), 7.39−7.32 (m, 3H), 3.77−3.74 (m, 2H), 3.62−3.59 (m, 2H), 1.67−1.54 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.9, 132.3, 129.8, 128.4, 120.7, 90.2, 81.4, 48.2, 42.3, 26.4, 25.3, 24.5. GC−MS (EI, 70 eV) *m/z*: 213 (43.23) $[M]^+$, 212 (45), 196 (8), 184 (20.5), 136 (14), 130 (12), 129 (100), 101 (12), 75 (14), 55 (7), 42 (6).

1-Morpholino-3-phenylprop-2-yn-1-one (**3am**).[5b,9g] White solid, mp 56−58 °C; 73.5 and 62.3 mg, 34 and 29% yield. ^1H NMR (400 MHz, $CDCl_3$): δ7.50−7.48 (m, 2H), 7.39−7.28 (m, 3H), 3.78 (dd, *J* = 5.4, 3.8 Hz, 2H), 3.70−3.68 (m, 2H), 3.64 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.1, 132.3, 130.1, 128.5, 120.2, 91.1, 80.7, 66.8, 66.4, 47.2, 41.9. GC−MS (EI, 70 eV) *m/z*: 215 (26.5) $[M]^+$, 186 (10.9), 130 (12.6), 129 (100), 116 (10), 101 (11.6), 75 (16.35), 56 (29.58).

3-Phenyl-1-(pyrrolidin-1-yl)prop-2-yn-1-one (**3an**).[9g,f] Yellowish oil; 89.5 mg,45% yield. ^1H NMR (400 MHz, $CDCl_3$): δ 7.51 (dd, *J* = 8.1, 1.4 Hz, 2H), 7.34 (dd, *J* = 7.2, 2.1 Hz, 3H), 3.70 (t, *J* = 6.4 Hz, 2H), 3.50 (t, *J* = 6.5 Hz, 2H), 1.97−1.88 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ152.7, 132.3, 129.9, 128.4, 120.6, 88.7, 82.6, 77.3, 77.0, 76.7, 48.1, 45.3, 25.3, 24.7. GC−MS (EI, 70 eV) *m/z*: 199 (39.5) $[M]^+$, 198 (15), 170 (18), 143 (10), 130 (11.1), 129 (100), 116 (12.39), 102 (19.81), 101 (12.5), 75 (16.3), 51 (6).

N,N-Dibutyl-3-(p-tolyl)propiolamide (**3ba**). Yellowish oil; 243.9 mg, 90% yield. ^1H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 8.1 Hz, 2H), 7.14 (d, *J* = 7.9 Hz, 2H), 3.60−3.54 (m, 2H), 3.40−3.34 (m, 2H), 2.35 (s, 3H), 1.62−1.50 (m, 4H), 1.40−1.29 (m, 4H), 0.93 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.5, 140.3, 132.2, 129.2, 117.7, 89.6, 81.7, 48.9, 44.5, 30.9, 29.5, 21.6, 20.2, 20.0, 13.9, 13.8.GC−MS (EI, 70 eV) *m/z*: 271 (2) $[M]^+$, 242 (3), 228 (11), 187 (4), 143 (100), 115 (8), 89 (4.5), 65 (2), 43 (2). HRMS (ESI) calcd for $[(C_{18}H_{25}NO)H]$ $[M + H]^+$: 272.2014, found 272.2009.

N,N-Dibutyl-3-(o-tolyl)propiolamide (**3ca**). Yellowish oil; 235.8 mg, 87% yield. ^1H NMR (500 MHz, $CDCl_3$): δ 7.50 (d, *J* = 7.6 Hz, 1H), 7.25 (m, 3H), 3.65−3.56 (m, 2H), 3.44−3.36 (m, 2H), 2.47 (s, 3H), 1.67−1.54 (m, 4H), 1.35 (m, 4H), 0.95 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 154.5, 141.1, 132.9, 129.8, 129.6, 125.7, 120.6, 88.3, 85.9, 49.0, 44.6, 31.1, 29.6, 20.7, 20.2, 20.0, 13.8. GC−MS (EI, 70 eV) *m/z*: 271 (5) $[M]^+$, 256 (12.5), 242 (10.5), 228 (14.5), 214 (10), 186 (6), 143 (100), 144 (15), 115 (43.7), 89 (8), 65 (3), 41 (6). HRMS (ESI) calcd for $[(C_{18}H_{25}NO)H]$ $[M + H]^+$: 272.2014, found 272.2009.

N,N-Dibutyl-3-(4-ethylphenyl)propiolamide (**3da**). Yellowish oil; 270.6 mg, 95% yield. ^1H NMR (400 MHz, $CDCl_3$): δ7.42 (d, *J* = 8.2 Hz, 2H), 7.16 (d, *J* = 8.2 Hz, 2H), 3.59−3.55 (m, 2H), 3.39−3.35 (m, 2H), 2.64 (q, *J* = 7.6 Hz, 2H), 1.64−1.51 (m, 4H), 1.37−1.29 (m, 4H), 1.21 (t, *J* = 7.6 Hz, 3H), 0.96−0.89 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ154.5, 146.5, 132.3, 128.0, 117.9, 89.6, 81.7, 77.3, 77.0, 76.7, 48.9, 44.5, 31.0, 29.6, 28.9, 20.2, 20.0, 15.1, 13.8, 13.8.GC−MS (EI, 70 eV) *m/z*: 285 (6) $[M]^+$, 242 (23.2), 201 (8), 200 (4), 157 (100), 142 (18), 114 (7), 77 (2), 44 (2). HRMS (ESI) calcd for $[(C_{19}H_{28}NO)H]$ $[M + H]^+$: 286.2171, found 286.2165.

N,N-Dibutyl-3-(4-propylphenyl)propiolamide (**3ea**). Yellowish oil; 281 mg, 94% yield. ^1H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, *J* = 8.1 Hz, 2H), 7.14 (d, *J* = 8.0 Hz, 2H), 3.59−3.50 (m, 2H), 3.41−3.34 (m, 2H), 2.62−2.54 (m, 2H), 1.62−1.21 (m, 10H), 0.99−0.87 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.5, 145.0, 132.2, 128.6, 117.9, 89.6, 81.7, 77.3, 48.9, 44.5, 38.0, 31.0, 29.6, 24.2, 20.2, 20.0, 13.8, 13.8, 13.7. GC−MS (EI, 70 eV) *m/z*: 299 (4) $[M]^+$, 270 (5), 256 (19), 214 (8), 200 (2.5), 171 (100), 157 (4), 142 (25), 114 (9.5), 84 (2), 57 (3), 41 (5). HRMS (ESI) calcd for $[(C_{20}H_{29}NO)H]$ $[M + H]^+$: 300.2327, found 300.2321.

N,N-Dibutyl-3-(4-methoxyphenyl)propiolamide (**3fa**). Yellowish oil; 264 mg, 92% yield. ^1H NMR (400 MHz, $CDCl_3$): δ 7.43 (d, *J* = 8.9 Hz, 2H), 6.84 (d, *J* = 8.9 Hz, 2H), 3.79 (s, 3H), 3.57−3.54 (m, 2H), 3.38−3.34 (m, 2H), 1.52−1.45 (m, 4H), 1.30 (m, 4H), 0.94−0.88 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ160.8, 154.7, 134.0, 114.1, 112.7, 89.8, 81.3, 77.3, 77.0, 76.7, 55.3, 48.9, 44.5, 30.9, 29.6, 20.1, 20.0, 13.8, 13.8.GC−MS (EI, 70 eV) *m/z*: 287 (6) $[M]^+$, 258 (8), 245 (10), 244 (15), 202 (13), 160 (13), 159 (100), 144 (10), 116 (6), 88 (2), 77 (2), 41 (4). HRMS (ESI) calcd for $[(C_{18}H_{25}NO)H]$ $[M + H]^+$: 288.1964, found 288.1958.

N,N-Dibutyl-3-(2-methoxyphenyl)propiolamide (**3ga**). Yellowish oil; 252.5 mg, 88% yield. ^1H NMR (500 MHz, $CDCl_3$): δ 7.50 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.36 (dd, *J* = 8.5 Hz, 1H), 6.95−6.86 (m, 2H), 3.86 (s, 3H), 3.67−3.63 (m, 2H), 3.42−3.37 (m, 2H), 1.64−1.55 (m, 4H), 1.42−1.31 (m, 4H), 0.97−0.92 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.0, 154.6, 134.3, 131.4, 120.5, 110.6, 110.1, 86.2, 85.9, 55.6, 48.9, 44.5, 31.0, 29.6, 20.2, 20.0, 13.8, 13.8. GC−MS (EI, 70 eV) *m/z*: 287 (2.5) $[M]^+$, 256 (29.5), 244 (12.3), 214 (10), 200 (9), 159 (100), 160 (12.7), 131 (21.5), 115 (34), 103 (10), 77 (17), 41 (5). HRMS (ESI) calcd for $[(C_{18}H_{25}NO)H]$ $[M + H]^+$: 288.1964, found 288.1958.

N,N-Dibutyl-3-(4-fluorophenyl)propiolamide (**3ha**). Yellowish oil; 239.2 mg, 87% yield. ^1H NMR (400 MHz, $CDCl_3$): δ 7.63−7.41 (m, 2H), 7.10−6.92 (m, 2H), 3.65−3.47 (m, 2H), 3.41−3.26 (m, 2H), 1.66−1.49 (m, 4H), 1.39−1.26 (m, 4H), 1.00−0.87 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ163.35 (d, $^1J_{C-F}$ = 251 Hz),154.3, 134.3 (d, $^3J_{C-F}$ = 10 Hz), 115.9 (d, $^2J_{C-F}$ = 22 Hz), 88.2, 81.9, 48.9, 44.6, 30.9, 29.5, 20.8, 19.9, 13.8, 13.8. GC−MS (EI, 70 eV) *m/z*: 275 (2) $[M]^+$, 232 (14), 218 (2), 191 (4), 147 (100), 119 (5), 99 (6), 41 (2.5). HRMS (ESI) calcd for $[(C_{17}H_{22}FNO)H]$ $[M + H]^+$: 276.1764, found 276.1761.

N,N-Dibutyl-3-(pyridin-3-yl)propiolamide (**3ia**). Yellowish brown oil; 162.5 mg, 63% yield. ^1H NMR (400 MHz, $CDCl_3$): δ 8.65 (d, *J* = 8.0 Hz, 2H), 7.79 (d, *J* = 7.9 Hz, 1H), 7.28 (dd, *J* = 7.1 Hz, 1H), 3.63−3.50 (t, 2H), 3.39−3.35 (t, 2H), 1.66−1.48 (m, 4H), 1.44−1.23 (m, 4H), 0.97−0.74 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.7, 152.5, 149.9, 139.2, 123.2, 85.6, 85.1, 48.9, 44.6, 30.9, 29.5, 20.1, 19.9, 13.8, 13.7. GC−MS (EI, 70 eV) *m/z*: 258 (2) $[M]^+$, 215 (17), 201 (3), 173 (5), 160 (2.5), 130 (100), 102 (10), 75 (5), 43 (3). HRMS (ESI) calcd for $[(C_{16}H_{22}N_2O)H]$ $[M + H]^+$: 259.1810, found 259.1805.

N,N-Dibutyl-3-(pyren-2-yl)propiolamide (**3ka**). Yellow oil; 339.9 mg, 89% yield. ^1H NMR (400 MHz, $CDCl_3$): δ 8.53 (d, *J* = 9.1 Hz, 1H), 8.26−8.01 (m, 8H), 3.78−3.73 (t, 2H), 3.50−3.46 (t, 2H), 1.81−1.73 (m, 2H), 1.66−1.62 (m, 2H), 1.51−1.35 (m, 4H), 1.02−0.95 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.6, 130.3, 129.0, 128.9, 127.1, 126.4, 126.1, 126.0, 125.0, 124.45, 114.8, 88.7, 87.5, 49.2, 44.7, 31.2, 29.7, 20.2, 20.1, 13.9, 13.9. HRMS (ESI) calcd for $[(C_{27}H_{27}NO)H]$ $[M + H]^+$: 382.2171, found 382.2165.

N,N-Dibutylnon-2-ynamide (**3la**). Colorless oil; 246.4 mg, 93% yield. ^1H NMR (400 MHz, $CDCl_3$): δ3.57−3.41 (m, 2H), 3.34−3.23 (m, 2H), 2.32 (t, *J* = 7.1 Hz, 2H), 1.64−1.21 (m, 18H), 0.99−0.81 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.6, 92.1, 74.5, 48.8, 44.4, 31.2, 30.9, 29.5, 28.5, 27.8, 22.4, 20.1, 19.9, 18.9, 14.0, 13.8, 13.7. GC−MS (EI, 70 eV) *m/z*: 265 (2.5) $[M]^+$, 266 (4), 250 (11), 236 (26.5), 222 (50), 208 (17), 166 (17), 137 (100), 86 (10), 67 (63.5), 55 (32), 43 (23), 41 (32.7). HRMS (ESI) calcd for $[(C_{17}H_{31}NO)H]$ $[M + H]^+$: 266.2484, found 266.2479.

N,N-Dibutyl-3-cyclopropylpropiolamide (**3ma**). Colorless oil; 207.7 mg, 94% yield. ^1H NMR (400 MHz, $CDCl_3$): δ3.50−3.39 (m, 2H), 3.37−3.25 (m, 2H), 1.54−1.21 (m, 10H), 0.9−0.83 (m, 8H), 0.81−0.79 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.5, 95.4, 69.7, 48.6, 44.3, 30.8, 29.5, 20.1, 19.9, 13.8, 13.8, 13.7, 8.8,-0.4.GC−MS (EI, 70 eV) *m/z*: 221 (1) $[M]^+$, 206 (4.3), 192 (5.3), 136 (8), 122 (5), 93 (100), 65 (17.6), 41 (6.4). HRMS (ESI) calcd for $[(C_{14}H_{23}NO)H]$ $[M + H]^+$: 222.1858, found 222.1854.

DOI: 10.1021/acs.joc.6b00386
J. Org. Chem. 2016, 81, 4974−4980

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00386.

^{1}H NMR and ^{13}C NMR spectral analysis (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: bm.bhanage@gmail.com, bm.bhanage@ictmumbai.edu.in. Phone: +91 2233612603. Fax: +91 2233611020.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

R.S.M. gratefully acknowledges the Council of Scientific & Industrial Research (CSIR), New Delhi, India, for the award of a Senior Research Fellowship (SRF).

■ REFERENCES

(1) (a) McDonald, I. M.; Mate, R. A.; Zusi, F. C.; Huang, H.; Post-Munson, D. J.; Ferrante, M. A.; Gallagher, L.; Bertekap, R. L., Jr.; Knox, R. J.; Robertson, B. J.; Harden, D. G.; Morgan, D. G.; Lodge, N. J.; Dworetzky, S. I.; Olson, R. E.; MacOr, J. E. *Bioorg. Med. Chem. Lett.* **2013**, *23*, 1684. (b) Eibl, C.; Tomassoli, I. b.; Munoz, L. c.; Stokes, C. d.; Papke, R. L. d.; Gundisch, D. *Bioorg. Med. Chem.* **2013**, *21*, 7309. (c) Pinto, A.; Neuville, L.; Retailleau, P.; Zhu, J. *Org. Lett.* **2006**, *8*, 4927.

(2) (a) Ryan, J.; Stang, P. *J. Org. Chem.* **1996**, *61*, 6162. (b) Hay, L.; Koenig, T.; Ginah, F.; Copp, J.; Mitchell, D. *J. Org. Chem.* **1998**, *63*, 5050. (c) Xie, X.; Lu, X.; Liu, Y.; Xu, W. *J. Org. Chem.* **2001**, *66*, 6545. (d) Peng, H.; Liu, G. *Org. Lett.* **2011**, *13*, 772. (e) Donets, P. A.; Van der Eycken, E. V. *Org. Lett.* **2007**, *9*, 3017.

(3) (a) Tohda, Y.; Sonogashira, K.; Hagihara, N. *Synthesis* **1977**, *1977*, 777. (b) Hoberg, H.; Riegel, H. *J. Organomet. Chem.* **1983**, *241*, 245. (c) Suda, T.; Noguchi, K.; Hirano, M.; Tanaka, K. *Chem. - Eur. J.* **2008**, *14*, 6593. (d) Lee, Y.; Motoyama, Y.; Tsuji, K.; Yoon, S.-H.; Mochida, I.; Nagashima, H. *ChemCatChem* **2012**, *4*, 778.

(4) (a) Rosenberg, S. H.; Rapoport, H. *J. Org. Chem.* **1985**, *50*, 3979. (b) Xu, W.; Kong, A.; Lu, X. *J. Org. Chem.* **2006**, *71*, 3854. (c) Donets, P. A.; Van Hecke, K.; Van Meervelt, L.; Van der Eycken, E. V. *Org. Lett.* **2009**, *11*, 3618.

(5) (a) Li, H.; Pan, C.; Cheng, Y.; Zhu, C. *Tetrahedron Lett.* **2013**, *54*, 6679. (b) Xie, Y.-X.; Song, R.-J.; Yang, X.-H.; Xiang, J.-N.; Li, J.-H. *Eur. J. Org. Chem.* **2013**, 5737. (c) Wu, J.-J.; Li, Y.; Zhou, H.-Y.; Wen, A.-H.; Lun, C.-C.; Yao, S.-Y.; Ke, Z.; Ye, B.-H. *ACS Catal.* **2016**, *6*, 1263.

(6) (a) Uenoyama, Y.; Fukuyama, T.; Nobuta, O.; Matsubara, H.; Ryu, I. *Angew. Chem.* **2005**, *117*, 1099. (b) Dhawan, R.; Dghaym, R. D.; St. Cyr, D. J.; Arndtsen, B. A. *Org. Lett.* **2006**, *8*, 3927. (c) Khedkar, M. V.; Sasaki, T.; Bhanage, B. M. *ACS Catal.* **2013**, *3*, 287. (d) Gautam, P.; Bhanage, B. M. *J. Org. Chem.* **2015**, *80*, 7810. (e) Mane, R. S.; Bhanage, B. M. *RSC Adv.* **2015**, *5*, 76122. (f) Mane, R. S.; Sasaki, T.; Bhanage, B. M. *RSC Adv.* **2015**, *5*, 94776.

(7) (a) Brennfuhrer, A.; Neumann, H.; Beller, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 4114. (b) Gadge, S. T.; Gautam, P.; Bhanage, B. M. *Chem. Rec.* **2016**, *16*, 835.

(8) For oxidative carbonylation reactions, see: (a) Gabriele, B.; Salerno, G.; Mancuso, R.; Costa, M. *J. Org. Chem.* **2004**, *69*, 4741. (b) Gabriele, B.; Plastina, P.; Salerno, G.; Mancuso, R.; Costa, M. *Org. Lett.* **2007**, *9*, 3319. (c) Orito, K.; Horibata, A.; Nakamura, T.; Ushito, H.; Nagasaki, H.; Yuguchi, M.; Yamashita, S.; Tokuda, M. *J. Am. Chem. Soc.* **2004**, *126*, 14342. (d) Brennfuhrer, A.; Neumann, H.; Beller, M. *ChemCatChem* **2009**, *1*, 28. (e) Liu, Q.; Zhang, H.; Lei, A. *Angew. Chem., Int. Ed.* **2011**, *50*, 10788. (f) Guan, Z.-H.; Chen, M.; Ren, Z.-H. *J. Am. Chem. Soc.* **2012**, *134*, 17490. (g) Xing, Q.; Shi, L.; Lang, R.; Xia, C.; Li, F. *Chem. Commun.* **2012**, *48*, 11023. (h) Gupte, S. P.; Chaudhari, R. V. *J. Catal.* **1988**, *114*, 246. (i) Li, F.; Xia, C. *J. Catal.* **2004**, *227*, 542. (j) Toochinda, P.; Chuang, S. C. *Ind. Eng. Chem. Res.* **2004**, *43*, 1192.

(9) (a) Fananas, F. J.; Hoberg, H. *J. Organomet. Chem.* **1984**, *277*, 135. (b) Hoberg, H.; Riegel, H. J. *J. Organomet. Chem.* **1983**, *241*, 245. (c) Gabriele, B.; Salerno, G.; Veltri, L.; Costa, M. *J. Organomet. Chem.* **2001**, *622*, 84. (d) Izawa, Y.; Shimizu, I.; Yamamoto, A. *Bull. Chem. Soc. Jpn.* **2004**, *77*, 2033. (e) Gadge, S. T.; Khedkar, M. V.; Lanke, S. R.; Bhanage, B. M. *Adv. Synth. Catal.* **2012**, *354*, 2049. (f) Zhang, C.; Liu, J.; Xia, C. *Catal. Sci. Technol.* **2015**, *5*, 4750. (g) Hwang, J.; Choi, J.; Park, K.; Kim, W.; Song, K. H.; Lee, S. *Eur. J. Org. Chem.* **2015**, *2015*, 2235. (h) Dong, Y.; Sun, S.; Yang, F.; Zhu, Y.; Zhu, W.; Qiao, H.; Wu, Y.; Wu, Y. *Org. Chem. Front.* **2016**, DOI: 10.1039/C6QO00075D.

(10) For palladium-catalyzed C−N bond activation, see: (a) Uehara, T. N.; Yamaguchi, J.; Itami, K. *Asian J. Org. Chem.* **2013**, *2*, 938. (b) Xie, Y.-J.; Hu, J.-H.; Wang, Y.-Y.; Xia, C.-G.; Huang, H.-M. *J. Am. Chem. Soc.* **2012**, *134*, 20613. (c) Li, M.-B.; Wang, Y.; Tian, S.-K. *Angew. Chem., Int. Ed.* **2012**, *51*, 2968. (d) Liu, Y.; Yao, B.; Deng, C.-L.; Tang, R.-Y.; Zhang, X.-G.; Li, J.-H. *Org. Lett.* **2011**, *13*, 2184. (e) Zhao, X.-H.; Liu, D.-L.; Guo, H.; Liu, Y.-G.; Zhang, W.-B. *J. Am. Chem. Soc.* **2011**, *133*, 19354. (f) Bao, Y.-S.; Zhaorigetu, B.; Agula, B.; Baiyin, M.; Jia, M. *J. Org. Chem.* **2014**, *79*, 803. (g) Murahashi, S.-I.; Hirano, T.; Yano, T. *J. Am. Chem. Soc.* **1978**, *100*, 348. (h) Murahashi, S.-I. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2443. (i) Ramachandiran, K.; Muralidharan, D.; Perumal, P. T. *Tetrahedron Lett.* **2011**, *52*, 3579.

(11) (a) Shi, R.; Lu, L.; Zhang, H.; Chen, B.; Sha, Y.; Liu, C.; Lei, A. *Angew. Chem., Int. Ed.* **2013**, *52*, 10582. (b) Fang, T.; Gao, X.-H.; Tang, R.-Y.; Zhang, X.-G.; Deng, C.-L. *Chem. Commun.* **2014**, *50*, 14775. (c) Shi, R.; Zhang, H.; Lu, L.; Gan, P.; Sha, Y.; Zhang, H.; Liu, Q.; Beller, M.; Lei, A. *Chem. Commun.* **2015**, *51*, 3247. (d) Yu, H.; Zhang, G.; Liu, Z.-J.; Huang, H. *RSC Adv.* **2014**, *4*, 64235.

(12) Mane, R. S.; Bhanage, B. M. *J. Org. Chem.* **2016**, *81*, 1223.

(13) (a) Gadge, S. T.; Bhanage, B. M. *J. Org. Chem.* **2013**, *78*, 6793. (b) Chavan, S. P.; Bhanage, B. M. *Tetrahedron Lett.* **2014**, *55*, 1199. (c) Gadge, S. T.; Kusumawati, E. N.; Harada, K.; Sasaki, T.; Hamane, D. N.; Bhanage, B. M. *J. Mol. Catal. A: Chem.* **2015**, *400*, 170. (d) Gadge, S. T.; Bhanage, B. M. *RSC Adv.* **2014**, *4*, 10367.

(14) Lee, J.; Park, J. *Org. Lett.* **2015**, *17*, 3960.

(15) (a) Ouyang, K.; Hao, W.; Zhang, W.-X.; Xi, Z. *Chem. Rev.* **2015**, *115*, 12045. (b) Yap, J. S. L.; Ding, Y.; Yang, X.-Y.; Wong, J.; Li, Y.; Pullarkat, S. A.; Leung, P.-H. *Eur. J. Inorg. Chem.* **2014**, *2014*, 5046. (c) Liu, Y.; Yao, B.; Deng, C.-L.; Tang, R.-Y.; Zhang, X.-G.; Li, J.-H. *Org. Lett.* **2011**, *13*, 2184. (d) Bao, Y.-S.; Zhaorigetu, B.; Agula, B.; Baiyin, M.; Jia, M. *J. Org. Chem.* **2014**, *79*, 803.

(16) (a) Yan, Y.; Xu, Y.; Niu, B.; Xie, H.; Liu, Y. *J. Org. Chem.* **2015**, *80*, 5581. (b) Gong, J.-L.; Qi, X.; Wei, D.; Feng, J.-B.; Wu, X.-F. *Org. Biomol. Chem.* **2014**, *12*, 7486. (c) Lu, L.; Xiong, Q.; Guo, S.; He, T.; Xu, F.; Gong, J.; Zhu, Z.; Cai, H. *Tetrahedron* **2015**, *71*, 3637.

DOI: 10.1021/acs.joc.6b00386
J. Org. Chem. 2016, 81, 4974−4980