JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

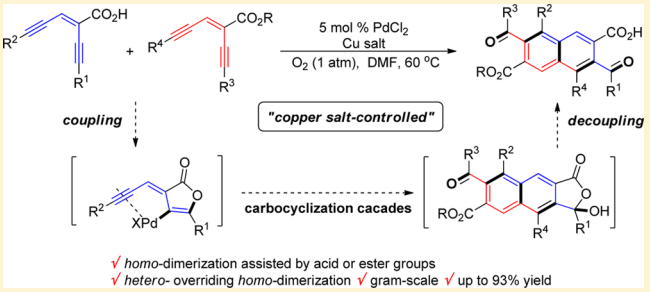
Coupling and Decoupling Approach Enables Palladium-Catalyzed Aerobic Bimolecular Carbocyclizations of Enediynes to 2,6-Diacylnaphthalenes

Fei Ling, Yanjun Wan, Dongxu Wang, and Cheng Ma*

Department of Chemistry, Zhejiang University, 20 Yugu Road, Hangzhou 310027, China

Supporting Information

ABSTRACT: A formal palladium-catalyzed aerobic bimolecular carbocyclization reaction of (*Z*)-hexa-1,5-diyn-3-ene scaffolds has been successfully developed for the construction of 2,6-diacylnaphthalenes, wherein copper salts play a critical role in accomplishing the oxygenative homo- and hetero-dimerization processes of readily accessible enediyne−carboxylic acids and esters, respectively. The enediyne dimerization protocol provides a flexible and regiospecific approach to a variety of functionalized naphthalenes with up to six differentiated substituents in good yields by using a directing-group-assisted coupling and decoupling strategy. Mechanistic studies indicated that the two oxygen atoms being selectively incorporated into the crossover-annulation products of enediynecarboxylic acid and ester directly originate from atmospheric molecular oxygen and H_2O, respectively.

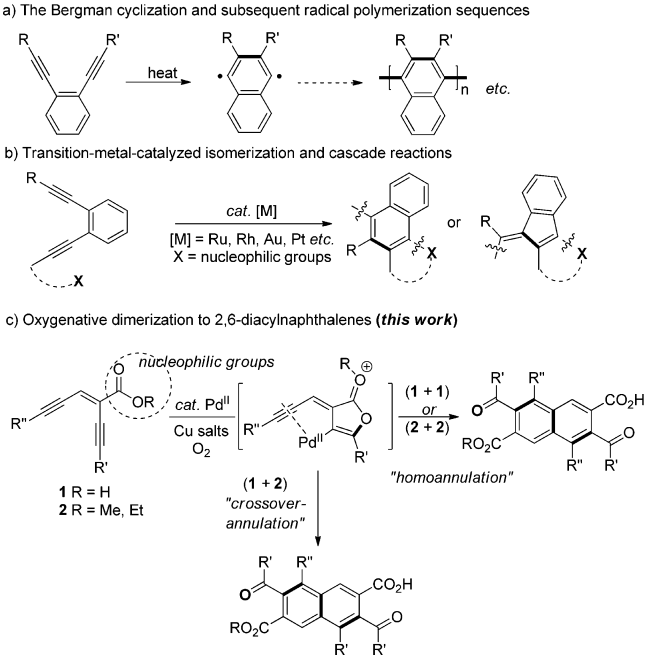


INTRODUCTION

Devising novel and efficient methods for the selective synthesis of polysubstituted naphthalene compounds is of great interest because of the prevalence of this structural motif in natural products and bioactive molecular as well as industry values.[1] In this context, the cycloaromatization and isomerization reactions of benzenoid enediynes provide a powerful tool for the construction of versatile naphthalene compounds. For instance, in light of the mechanistic proposal for the formation of polymeric byproducts in the classic Bergman cyclization,[2] the thermotriggered isomerization and polymerization of acyclic enediynes was endeavored and has become as a promising strategy for the generation of conjugated aromatic polymers bearing naphthalene skeletons (Scheme 1a).[3] Meanwhile, a set of elegant radical-induced polycyclizations of well-designed oligo(phenylene-1,2-ethynylenes) have recently been established to deliver nanoscale aromatic ribbons.[4] In addition to these radical-mediated cycloaromatization reactions, transition-metal-catalyzed cycloisomerizations of enediynes have been notably investigated in the past decade, offering a variety of efficient methods to construct substituted naphthalene compounds as well as other aromatic molecules under mild reaction conditions (Scheme 1b).[5,6]

Despite significant progress in their cycloisomerization and intramolecular cyclization reactions, very limited attention has been devoted to the intermolecular carbocyclization of enediyne scaffolds, which would allow more flexible formations of substituted aromatics from simple substrates. To the best of our knowledge, there are only a few precedents in the literature that address the intermolecular [4 + 2] cyclization of enediyne compounds with C2 components like α-hydroxy ketones[7a] and simple alkynes.[7b] In this case, given the multiple unsaturated C−C bonds of enediynes, many troublesome problems

Scheme 1. Annulations of Acyclic Enediynes to Naphthalenes



Received: December 22, 2015
Published: March 8, 2016

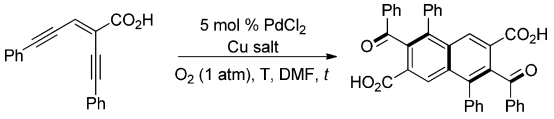
DOI: 10.1021/acs.joc.5b02870
J. Org. Chem. 2016, 81, 2770−2781

associated with reaction selectivity[8] need to be overcome in addition to the innate isomerization obstacle of this structural motif. Triggered by our previous results on the Pd/Cu-catalyzed aerobic [4 + 2] benzannulation between enediyne carboxylic compounds and internal alkynes,[7b] we have attempted to handle the dimerization reaction of enediynes[9] and found that a class of 2,6-diacylnaphthalenes[10] could be directly assembled through a formal palladium/copper-catalyzed intermolecular oxygenative carbocyclization of enediyne skeletons (Scheme 1c).[11] Remarkably, it appeared that copper salts play a critical role in controlling the reaction selectivity beyond an oxidant in the directing-group-assisted palladium-catalyzed aerobic cascade cyclization of enediyne-carboxylic acids **1** and enediynecarboxylic esters **2**.[12]

RESULTS AND DISCUSSION

Initial studies on enediyne homodimerization were started with readily accessible enediyne−acid **1a** by using $PdCl_2$ (10 mol %) as the catalyst in the presence of $CuBr_2$ (20 mol %) in DMF under 1 atm of O_2 (Table 1). While a sluggish conversion of **1a**

Table 1. Optimization of Reaction of Acids 1[a]



1a **3a**

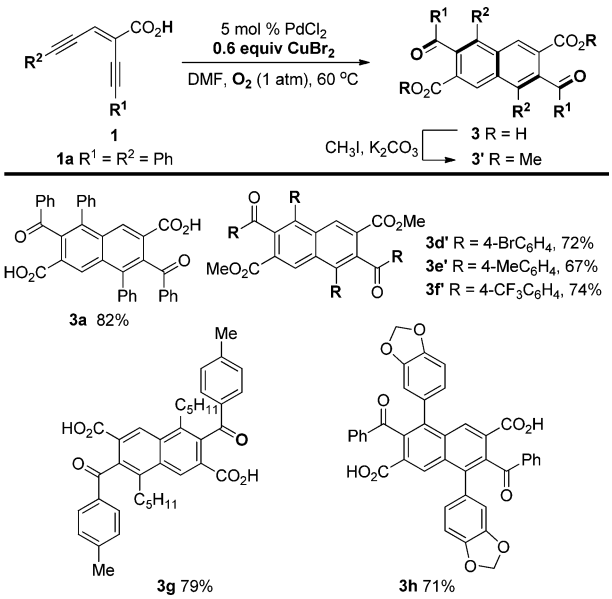
entry	Cu salt (equiv)	time (h)	T (°C)	yield[b] (%)
1	$CuBr_2$ (0.2)	8	35	7
2	$CuBr_2$ (0.2)	8	60	22
3	$Cu(OAc)_2$ (0.2)	8	60	trace
4	$CuCl_2$ (0.2)	8	60	trace
5	$Cu(OTf)_2$ (0.2)	8	60	13
6	CuBr (0.2)	8	60	trace
7	CuI (0.2)	8	60	15
8	**$CuBr_2$ (0.6)**	**4**	**60**	**82**
9	$CuBr_2$ (1.0)	3	60	74
10[c]	$CuBr_2$ (0.2)	12	60	

[a]Unless otherwise noted, the reaction was carried out using **1a** (0.1 mmol), $PdCl_2$ (5 mol %), and Cu salts in DMF (1.0 mL) under O_2 (1 atm). [b]Isolated yield. [c]In the absence of $PdCl_2$.

occurred at 35 °C, it appeared that **1a** was too labile to be converted into a highly complex mixture involving naphthoic diacid **3a** at elevated temperature (Table 1, entries 1 and 2). Switching $CuBr_2$ to a set of other copper salts did not improve the product yield (Table 1, entries 3−7). After exhaustive efforts on optimization of reaction conditions, a key breakthrough was ultimately achieved by identifying that not only the copper salts employed but also the amount of Cu co-catalyst is critical for completing a clear conversion of **1a** to give naphthoic diacid **3a**. In the presence 5 mol % of $PdCl_2$ and $CuBr_2$ (0.6 equiv), **1a** underwent this dimerization−oxygenation cascade smoothly in DMF at 60 °C in O_2 (1 atm), affording **3a** in 82% yield after 4 h (Table 1, entry 8). Nevertheless, further increasing the amount of $CuBr_2$ from 0.6 equiv to 1.0 equiv would result in a decreasing yield (74%) because of the generation of some undetermined byproducts (Table 1, entry 9). In contrast, no desired product was detected in the absence of any palladium catalysts (Table 1, entry 10).

With the optimal reaction conditions in hand, the scope of the oxygenative homodimerization of acids **1** was examined (Scheme 2). Accordingly, variation of substituents R^1 or R^2 of acids **1** indicated that a set of benzene rings with an electron-

Scheme 2. Oxygenative Homo-dimerization of Acids 1[a]



[a]The reaction was carried out on a 0.2 mmol scale of acids **1** with $PdCl_2$ (5 mol %), and $CuBr_2$ (0.6 equiv) in DMF (2.0 mL) under O_2 (1 atm) at 60 °C. The yields are of the isolated products.

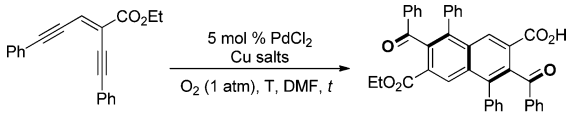
donating group (−Me) or an electron-withdrawing group ($-CF_3$) as well as a halogen (−Br) were well tolerated to form a broad array of C_2-symmetric naphthoic diacids of potential interest in functional materials and supramolecular architectures.[13] Due to the poor solubility of acids **3d**, **3e**, and **3f**, their corresponding ester derivatives **3d′**, **3e′**, and **3f′** were produced as products upon treatment with CH_3I under basic conditions. The alkyl group ($-C_5H_{11}$) was also completely compatible with the catalytic systems to afford **3g** in 79% yield. In addition, the benzene ring could be effectively replaced by other aromatic substituents like benzo[*d*][1,3]dioxol-5-yl to forge the desired naphthalene product **3h** in good yield.

Intriguingly, when enediyne−ester **2a** was subjected to $PdCl_2$ (5 mol %) and $CuBr_2$ (0.6 equiv) in DMF at 60 °C under oxygen atmosphere, a partially hydrolyzed product of 2,6-diacylnaphthalene **4a** was isolated in 35% yield after 12 h (Table 2, entry 1).[14] Reducing the amounts of copper salts improved the yield of **4a** (Table 2, entry 2). Using 0.2 equiv of $CuCl_2$ instead of $CuBr_2$ not only sharply improved the product yield but also accelerated this transformation of **2a**, giving access to **4a** in 83% yield after 6 h (Table 2, entry 3). However, replacing $CuBr_2$ with a set of other copper salts disfavored the formation of product **4a**. For example, while a relatively lower yield of **4a** was found with CuCl as the co-catalyst, $Cu(OAc)_2$ only delivered traceless product (Table 2, entries 4 and 5). Further studies indicated that the reaction temperature had little effect on this reaction, and lowering or elevating the reaction temperature would decrease the yield of **4a** (Table 2, entries 6 and 7). As expected, no desired product was detected in the absence of $PdCl_2$, suggesting that palladium catalyst is critical to this transformation of enediyne−ester **2a** (Table 2, entry 8).

A survey on the substrate scope of esters **2** is shown in Scheme 3. A variety of functional groups including halogen (**4c′**

DOI: 10.1021/acs.joc.5b02870
J. Org. Chem. 2016, 81, 2770−2781

Table 2. Optimization of Reaction of 2a[a]

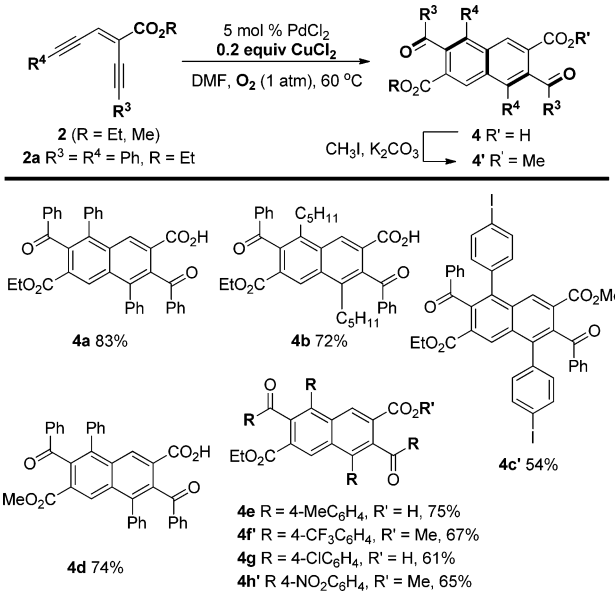


2a 4a

entry	Cu salt	time (h)	T (°C)	yield (%)[b]
1[c]	$CuBr_2$	12	60	35
2	$CuBr_2$	12	60	47
3	**$CuCl_2$**	**6**	**60**	**83**
4	$Cu(OAc)_2$	12	60	trace
5	CuCl	8	60	59
6	$CuCl_2$	4	80	66
7	$CuCl_2$	24	30	33
8[c,d]	$CuCl_2$	12	60	

[a]Unless otherwise noted, the reaction was carried out using **2a** (0.1 mmol), Pd catalyst (5 mol %), and Cu salts (0.2 equiv) in DMF (1.0 mL) under O_2 (1 atm). [b]Isolated yield. [c]$CuBr_2$ (0.6 equiv). [d]Without $PdCl_2$

Scheme 3. Oxygenative Homo-dimerization of Esters 2[a]

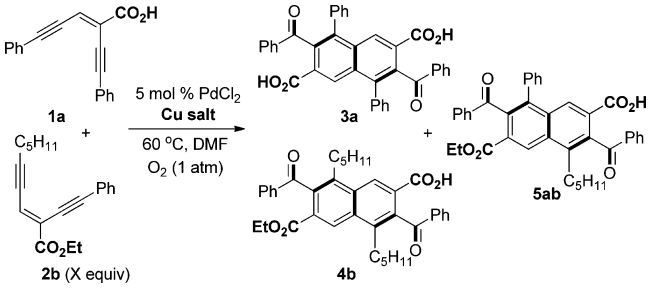


[a]Unless otherwise noted, the reaction was carried out on a 0.2 mmol scale of acids **2** with $PdCl_2$ (5 mol %), and $CuCl_2$ (0.2 equiv) in DMF (2.0 mL) under O_2 (1 atm) at 60 °C. The yields are of the isolated products.

and **4g**), trifluoromethyl (**4f′**), and nitro groups (**4h′**) were applicable for the current catalytic system, providing good yields of the targeted naphthalene products **4**. An alkyl group (1-pentyl) could be employed in this reaction to give **4b** in 72% yield. Moreover, methyl ester **2d** (R^3 = R^4 = Ph, R = Me) also underwent this reaction smoothly, affording **4d** in good yield. In addition, the structure of **4h′** was unambiguously determined by single-crystal X-ray analysis.

Given the different reactivities of enediyne acid **1a** and ester **2a** upon treatment with $CuBr_2$ in the Pd-catalyzed aerobic annulation reaction, we envisioned that the choice of suitable copper salts might enable a selective crossover-annulation of **1** and **2**, which constituted a pair of ideal reaction partners for the construction of diverse substituted naphthalene products (Table 3). Thus, a mixture of acid **1a** and ester **2b** (3.0

Table 3. Optimization of Reaction of 1a and 2b[a]



entry	2b[b] (equiv)	Cu salt (equiv)	time (h)	yield[c,d] (%) of 3a/4b/5ab
1	3.0 (1.5)	$CuBr_2$ (0.2)	3.5	15/5/67
2	3.0 (1.1)	$CuCl_2$ (0.2)	2.0	16/7/59
3	3.0 (2.7)	$Cu(OAc)_2$ (0.2)	12	<5/<5/<5
4	3.0 (2.1)	CuBr (0.2)	10	10/13/21
5	3.0 (2.1)	CuI (0.2)	2.0	<5/<3/<72
6	3.0 (1.8)	CuI (0.6)	1.0	<5/<3/88
7	3.0 (1.8)	CuI (1.0)	0.75	<5/<3/92
8	2.0 (1.0)	CuI (1.0)	0.75	7/<3/84
9	1.5 (0.4)	CuI (1.0)	0.75	11/<3/73
10[e]	3.0 (1.8)	CuI (1.0)	2	22/9/67
11	3.0 (−)	none	12	31/30/30
12	3.0 (2.9)	CuI (1.0)	12	nr

[a]Unless otherwise noted, reactions were conducted at 60 °C on a 0.2 mmol scale of **1a** with **2b**, $PdCl_2$ (5 mol %), and Cu salts in DMF (2.0 mL) under O_2 (1 atm). [b]Amounts of recovered **2b** in parentheses. [c]Isolated yields. [d]The yield of **4b** was determined according to **2b** consumed, while those of **3a** and **5ab** referred to **1a**. [e]In 10:1 DMF/H_2O. nr = no reaction.

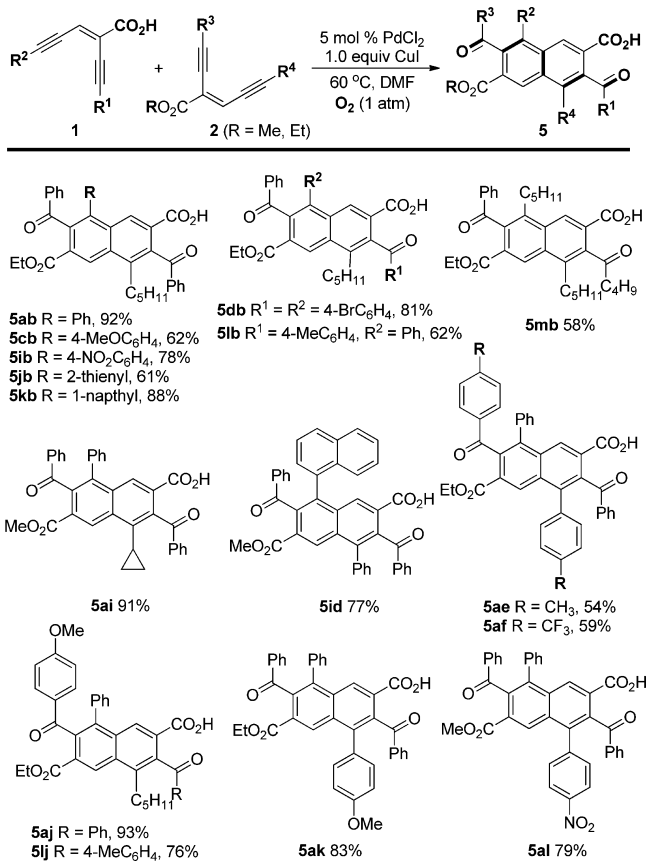
equiv) was subjected to $PdCl_2$ (5 mol %) and a set of Cu salts in DMF at 60 °C under 1 atm of O_2. To our delight, when 0.2 equiv of $CuBr_2$ was used as the co-catalyst, cross-dimerization product **5ab** was isolated in 67% yield, along with some homodimers of **3a** and **4b** (Table 3, entry 1). After a series of Cu^{II} and Cu^{I} salts were screened, CuI ws found to be optimal, not only providing the highest yield but also inhibiting the generation of homodimers, especially of **3a** (Table 3, entries 2−5). Excess amounts of **2b** could be recovered after the reaction, which is favorable to large-scale manipulation. Increasing the loading of CuI from 0.2 to 0.6 or 1.0 equiv could accelerate the conversion and afforded **5ab** in 88% and 92% yield, respectively (Table 3, entries 6 and 7), whereas raising the ratio of **1a** to **2b** prompted the homodimerization of **1a**, and the heterodimer **5ab** was still obtained as the major product by using 2 equiv or even 1.5 equiv of ester **2b** (Table 3, entries 8 and 9). It was also observed that an aqueous solvent system (DMF/H_2O = 10:1) had little influence on reaction outcomes (Table 3, entry 10). Notably, in the absence of Cu salts, a complicated mixture involving dimers **3a**, **4b**, and **5ab** could still be formed but in low yields without any selectivity (Table 3, entry 11). Nevertheless, no productive conversions were observed in the absence of $PdCl_2$ (Table 3, entry 12). All of these results clearly indicated that Cu salts play an important role in facilitating this Pd-catalyzed aerobic crossover-annulation cascade selectively, presumably due to the difference in the coordinating ability of substrates and the product to copper ions as well as the ligand exchange of palladium catalyst with the counterion of copper salts.[15]

After optimal conditions for this aerobic heterodimerization reaction were identified, diverse sets of acids **1** and esters **2**

DOI: 10.1021/acs.joc.5b02870
J. Org. Chem. 2016, 81, 2770−2781

were evaluated (Scheme 4). A set of acids **1** were able to react with ester **2b** selectively to deliver naphthoic acids **5**. Generally

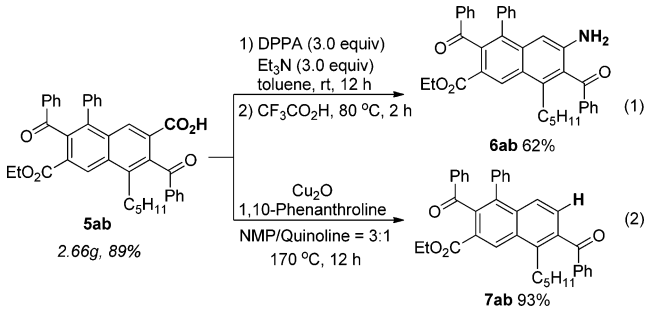
Scheme 4. Substrate Scopes of 1 and 2[a]



[a]Reactions were conducted at 60 °C on a 0.2 mmol scale of **1a** with **2b** (0.6 mmol), $PdCl_2$ (5 mol %), and CuI (1 equiv) in DMF (2.0 mL) under O_2 (1 atm). The yields are of the isolated products.

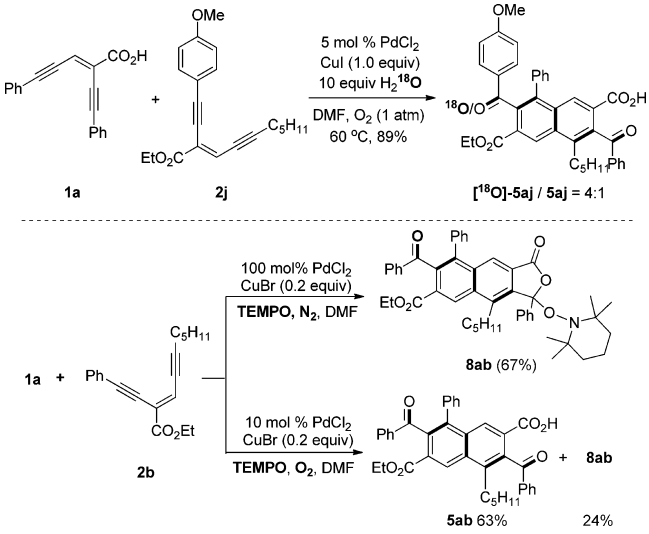
good yields and high selectivity were observed for a wide scope of aryl-substituted acids **1** possessing different electronic properties on the benzene rings. Electron-donating groups (−Me and −OMe) and electron-withdrawing group ($-NO_2$ and −Br) were wholly tolerated. Other aromatic rings, such as 2-thienyl and 1-naphthyl, were also effective for this process, leading to the synthesis of **5jb** and **5kb** in 61% and 88% yields, respectively. Moreover, an alkyl-substituted substrate could be introduced to this reaction to form **5mb** in 58% yield. On the other hand, the scope of esters **2** was also examined. As expected, good yields were obtained for methyl ester partners (**5ai** and **5id**). Both electron-rich and electron-poor aryl substituents tethered to the termini of enediynes **2** had little effect on this conversion, for example, producing **5ak** and **5al** in similar yields. Perhaps most remarkable is the capacity of this method to enable the assembly of fully differentiated hexasubstituted naphthalenes in a regioisomer-free manner, as shown by the formation of **5lj** in 76% isolated yield.

The oxygenative dimerization reaction could be easily carried out on a multigram scale, for example, to produce acid **5ab** in 89% yield. The resulting product potentially offered a versatile platform for the synthesis of polysubstitued naphthalene compounds. Further conversion of the carboxylic acid group of **5ab** to an amine afforded **6ab** in 62% yield through a Curtius rearrangement and hydrolyzation sequence (eq 1), while the copper-catalyzed protodecarboxylation gave access to ester **7ab** (eq 2).



To explore the mechanism of the heterodimerization of acids **1** and esters **2**, control experiments with $H_2{}^{18}O$ isotopic labeling and an radical scavenger 2,2,6,6-tetramethyl-1-piperidine-1-oxyl (TEMPO) were performed (Scheme 5). An entry

Scheme 5. Control Experiments

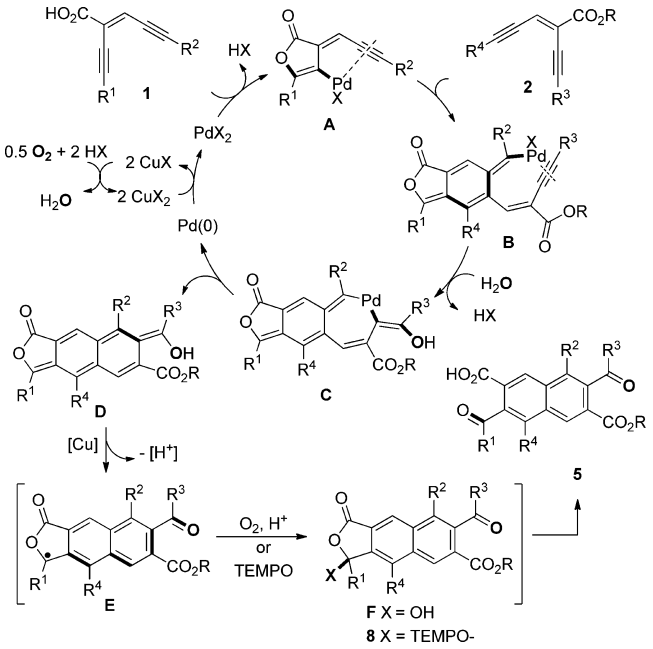


in the presence of $H_2{}^{18}O$ under O_2 afforded [^{18}O]-**5aj** and **5aj** (4:1) in 89% combined yield, suggesting that the ketonic oxygen adjacent to the ester group comes from H_2O directly, while the other comes from O_2. Incomplete incorporation of the ^{18}O label was likely due to the competing attack of both adventitious water and in situ generated water arising from catalyst regeneration with O_2 as the reoxidant. Moreover, in the presence of stoichiometric TEMPO, whereas a mixture of **5ab** (63%) and TEMPO adduct **8ab** (24%) was obtained under O_2, an entry under N_2 could furnish **8ab** in 67% yield. These results clearly indicated that a radical species was involved and would be responsible for the subsequent oxygen-incorporation sequence using O_2.[16]

A tentative mechanism for the synthesis of 2,6-diacylnaphthalenes **5** is depicted in Scheme 6. Thus, initial intramolecular cyclization of enediyne **1** via a 5-*endo-dig anti*-aminopalladation forms vinylpalladium species **A**,[17] which undergoes a sequential 2-fold carbopalladation cascade selectively with one alkyne moiety of **2** to give intermediate **B**. It is proposed that the ester group of enediynes **2** might be capable of differentiating their two alkyne moieties for the cross-coupling sequence. The nucleophilic addition of H_2O onto to **B** followed by a reductive elimination would liberate putative polyenol **D** and a Pd^0

DOI: 10.1021/acs.joc.5b02870
J. Org. Chem. 2016, 81, 2770−2781

Scheme 6. Tentative Reaction Mechanism



species,[18] which can be oxidized to the active Pd^{II} catalyst using O_2 as reoxidants. Subsequent Cu-mediated one-electron oxidation of the enol moiety of **D** followed by aromatization would then afford radical **E**.[19] Thereafter, **E** would be interrupted by O_2 to produce intermediate **F**, presumably through Fenton-type fragmentation of intermediate superoxo radicals.[20] Spontaneous ring−chain tautomerism of **F** proceeds to give the product **5**. On the other hand, trapping of the radical **E** with TEMPO would furnish adduct **8**.

CONCLUSIONS

In summary, we have developed a novel palladium/copper-catalyzed formal oxygenative bimolecular annulation of non-benzenoid enediyne scaffolds using atmospheric molecular oxygen as the oxygen source and reoxidant under mild conditions. It is found that copper salts play a critical role to facilitate the present palladium-catalyzed homo- and hetero-dimmerization of readily accessible enediyne−carboxylic acids and esters with excellent selectivity by using a directing-group-assisted coupling and decoupling strategy[21] to interrupt the innate cycloisomerization tendency of enediyne subunits. This efficient protocol possesses the capability of constructing a class of functionalized naphthalenes containing up to six differentiated substituents in a regioisomer-free manner and might find synthetic application in the future.

EXPERIMENTAL SECTION

General Experimental Methods. All reactions were carried out under oxygen atmosphere with dry, freshly distilled solvents in anhydrous conditions. DMF was distilled from CaH_2 immediately prior to use. All chemicals were used without further purification as commercially available unless otherwise noted. Thin-layer chromatography (TLC) was performed on silica gel plates (60F−254) using UV light (254 and 365 nm). Flash chromatography was conducted on silica gel (300−400 mesh). NMR (400 or 600 MHz for ^1H NMR, 100 or 150 MHz for ^{13}C NMR) spectra were recorded in $CDCl_3$ with TMS as the internal standard unless otherwise noted. HRMS were recorded using EI-TOF or ESI-TOF techniques.

General Procedure for the Preparation of Starting Materials. **Procedure A for Acids 1.** K_2CO_3 (276.4 mg, 2.0 mmol) and iodomethane (125 μL, 2.0 mmol) were added to a stirred solution of the corresponding enediyne imide[9a] (1.0 mmol) in DMF (4.0 mL). After 3 h, the solution was evaporated, water (20 mL) was added, and the resulting mixture was extracted with EtOAc (3 × 5 mL). The combined organic layers were dried over Na_2SO_4, filtrated, and evaporated. The crude product was purified by silica gel chromatography using petroleum ether/ethyl acetate = 10:1 as the eluent to give the *N*-methyl product. The *N*-methyl product was then added to an aqueous solution of NaOH (6 M, 10 mL). The mixture was heated and stirred at 85 °C for 2 h, cooled to room temperature, acidified with a solution of HCl (3 M), and extracted with ethyl acetate (2 × 10 mL). The combined organic layers were dried over Na_2SO_4, filtrated, and evaporated. The crude product was purified by silica gel chromatography using petroleum ether/ethyl acetate = 1:1 as the eluent to give acids **1**. **Procedure B for Esters 2.** K_2CO_3 (276.4 mg, 2.0 mmol) and iodomethane (125 μL, 2.0 mmol) were added to a stirred solution of the corresponding enediyne imide (1.0 mmol) in DMF (4.0 mL). After 3 h, the solution was evaporated, water (20 mL) was added, and the resulting mixture was extracted with EtOAc (3 × 5 mL). The combined organic layers were dried over Na_2SO_4, filtrated, and evaporated. The crude product was purified by silica gel chromatography using petroleum ether/ethyl acetate = 10:1 as the eluent to give the *N*-methyl product. Then the *N*-methyl product was added to a solution of NaOEt (2.0 mmol) in EtOH (4.0 mL) under N_2 at 0 °C. The mixture was stirred at 25 °C for 20 min; water (10 mL) was added and the mixture extracted with ethyl acetate (2 × 10 mL). The combined organic layers were dried over Na_2SO_4, filtrated, and evaporated. The crude product was purified by silica gel chromatography using petroleum ether/ethyl acetate = 10:1 as the eluent to give ester **2**. **Procedure C for Acids 1 and Esters 2.** Et_3N (810.0 mg, 8.0 mmol) was added to a stirred solution of (*Z*)-2,3-dibromoacrylic ester (2.0 mmol) and $PdCl_2(PPh_3)_2$ (42.1 mg, 0.6 mmol %) in THF (4.0 mL). After the solution was stirred at 25 °C for 10 min, alkyne (6.0 mmol) and CuI (19.0 mg, 0.1 mmol) were added sequentially, and then the reaction was allowed to warm to 60 °C for 1 h. Saturated NH_4Cl was added, and the resulting mixture was extracted with DCM (3 × 5 mL). The combined organic layers were dried over Na_2SO_4, filtrated, and evaporated. The crude product was purified by silica gel chromatography using petroleum ether/ethyl acetate = 20:1 as the eluent to give the ester product **2**. Then KOH powder (224.0 mg, 4 mmol) was added to the solution of the ester **2** in EtOH (5 mL), and the reaction was stirred at 25 °C for 2 h. The solvent then was evaporated, and water (10 mL) was added. The mixture was washed with diethyl ether (3 × 5 mL), and the aqueous phase was acidized by HCl (2 M) and extracted ethyl acetate (3 × 5 mL). The combined organic layers were dried over Na_2SO_4, filtrated, and evaporated to afford acid **1**. **Procedure D for Acids 1 and Esters 2.** Et_3N (405.0 mg, 4.0 mmol) was added to a stirred solution of (*Z*)-ethyl-2,3-dibromoacrylate (2.0 mmol) and $PdCl_2(PPh_3)_2$ (42.1 mg, 0.6 mmol %) in THF (4.0 mL). After the solution was stirred at 25 °C for 10 min, alkylalkyne (4.0 mmol) and CuI (19.0 mg, 0.1 mmol) were added sequentially, and then the reaction was allowed to stir at 25 °C for 5 h. Then another alkyne (4.0 mmol), Et_3N (405.0 mg, 4.0 mmol), $PdCl_2(PPh_3)_2$ (42.1 mg, 0.6 mmol %), and CuI (19.0 mg, 0.1 mmol) were added. The mixture was stirred for 4 h, saturated NH_4Cl was added, and the resulting mixture was extracted with DCM (3 × 5 mL). The combined organic layers were dried over Na_2SO_4, filtrated, and evaporated. The crude product was purified by silica gel chromatography using petroleum ether/ethyl acetate = 20:1 as the eluent to give the ester product. Then KOH powder (224.0 mg, 4 mmol) was added to the solution of the ester product in EtOH (5 mL), and the reaction was stirred at 25 °C for 2 h. The solvent then was evaporated, and water (10 mL) was added. The mixture was washed with diethyl ether (3 × 5 mL), and the aqueous phase was acidified by HCl (2 M) and extracted ethyl acetate (3 × 5 mL). The combined organic layers were dried over Na_2SO_4, filtrated, and evaporated to afford acid **1**. **Procedure E for Esters 2.** To a solution of acid **1** (0.2 mmol) in DMF (2 mL) were added MeI (56.8 mg, 0.4 mmol) and K_2CO_3 (55.3

DOI: 10.1021/acs.joc.5b02870
J. Org. Chem. 2016, 81, 2770−2781

mg, 0.4 mmol), and the mixture was stirred at 40 °C for 6 h. Then the solvent was evaporated, water (5 mL) was added, and the resulting mixture was extracted with ethyl acetate (3 × 5 mL). The combined organic layers were dried over Na_2SO_4, filtrated, and evaporated. The crude product was purified by silica gel chromatography using petroleum ether/ethyl acetate = 10:1 as the eluent to give ester **2**.

*(E)-2-(Phenylethynyl)dec-2-en-4-ynoic Acid (**1b**).* Prepared according to procedure D in 69% yield over three steps (367.5 mg): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 10.6 (s, 1H), 7.47−7.44 (m, 2H), 7.27−7.25 (m, 3H), 7.02−7.01 (m, 1H), 2.48−2.44(m, 2H), 1.59−1.51 (m, 2H), 1.39−1.32 (m, 2H), 1.28−1.19 (m, 2H), 0.79 ppm (m, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 169.7, 131.9, 130.2, 128.9, 128.3, 123.2, 122.6, 110.5, 98.3, 83.8, 78.9, 31.0, 28.1, 22.2, 20.5, 13.9; HRMS (EI) m/z [M]$^+$ calcd for $C_{18}H_{18}O_2$ 266.1307, found 266.1313.

*(E)-5-(4-Methoxyphenyl)-2-(phenylethynyl)pent-2-en-4-ynoic Acid (**1c**).* Prepared according to procedure A in 75% yield over two steps (226.7 mg): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 13.39 (s, 1H), 7.56−7.46 (m, 7H), 7.21 (s, 1H), 7.05 (d, J = 7.2 Hz, 2H), 3.82 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 164.5, 160.7, 133.6, 131.3, 129.4, 129.0, 126.8, 124.2, 121.9, 114.8, 113.2, 105.4, 98.1, 86.8, 85.4, 55.4; HRMS (EI) m/z [M]$^+$ calcd for $C_{20}H_{14}O_3$ 302.0943, found 302.0946.

*(E)-5-(4-Bromophenyl)-2-((4-bromophenyl)ethynyl)pent-2-en-4-ynoic Acid (**1d**).* Prepared according to the typical procedure C in 72% yield over two steps (619.3 mg): ^{1}H NMR (400 MHz, DMSO, 25 °C, TMS) δ = 13.56 (s, 1H), 7.70−7.66 (m, 4H), 7.50−7.47 (m, 4H), 7.23 ppm (s, 1H); ^{13}C NMR (100 MHz, DMSO, 25 °C, TMS) δ = 164.1, 133.6, 133.3, 132.2, 132.1, 126.4, 125.7, 123.8, 123.1, 120.8, 120.5, 103.2, 97.5, 88.3, 86.3; HRMS (EI) m/z [M]$^+$ calcd for $C_{19}H_{10}Br_2O_2$ 427.9048, found 427.9049.

*(E)-5-(p-Tolyl)-2-(p-tolylethynyl)pent-2-en-4-ynoic Acid (**1e**).* Prepared according to the typical procedure C in 72% yield over two steps (432.5 mg): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 7.410−7.36 (m, 4H), 7.19 (s, 1H), 7.11 (d, J = 6.8 Hz, 4H), 2.31 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 169.4, 140.4, 139.4, 132.2, 131.8, 129.4, 129.2, 128.6, 123.3, 119.6, 119.3, 107.4, 99.8, 87.3, 83.7, 21.7, 21.7; HRMS (EI) m/z [M]$^+$calcd for $C_{21}H_{16}O_2$ 300.1150, found 300.1153.

*(E)-5-(4-(Trifluoromethyl)phenyl)-2-((4-(trifluoromethyl)phenyl)-ethynyl)pent-2-en-4-ynoic Acid (**1f**).* Prepared according to the typical procedure C in 53% yield over two steps (432.8 mg): ^{1}H NMR (400 MHz, DMSO, 25 °C, TMS) δ = 13.70 (s, 1H), 7.86−7.83 (m, 4H), 7.79−7.76 (m, 4H), 7.33 ppm (s, 1H); ^{13}C NMR (100 MHz, DMSO, 25 °C, TMS) δ = 163.9, 132.5, 132.2, 129.6 (q, J = 44.6 Hz), 126.8, 126.3, 130.0 (q, J = 18.1 Hz), 125.9, 125.9, 125.9, 125.8, 125.4, 125.2 (q, J = 269.9 Hz), 102.5, 97.1, 89.0, 87.2; HRMS (EI) m/z [M]$^+$ calcd for $C_{21}H_{10}F_6O_2$ 408.0585, found 408.0587.

*(E)-5-(Benzo[d][1,3]dioxol-5-yl)-2-(phenylethynyl)pent-2-en-4-ynoic Acid (**1h**).* Prepared according to the typical procedure A in 66% yield over two steps (208.8 mg): ^{1}H NMR (400 MHz, DMSO, 25 °C, TMS) δ = 13.41 (s, 1H), 7.54−7.47 (m, 5H), 7.18−7.01 (m, 4H), 6.12 ppm (s, 2H); ^{13}C NMR (100 MHz, DMSO, 25 °C, TMS) δ = 164.5, 149.2, 147.6, 131.3, 129.4, 129.0, 127.3, 126.4, 124.8, 121.8, 114.4, 111.0, 109.1, 105.1, 101.9, 98.2, 86.4, 85.4; HRMS (EI) m/z [M]$^+$ calcd for $C_{20}H_{12}O_4$ 316.0736, found 316.0733.

*(E)-5-(4-Nitrophenyl)-2-(phenylethynyl)pent-2-en-4-ynoic Acid (**1i**).* Prepared according to procedure A in 56% yield over two steps (177.7 mg); ^{1}H NMR (400 MHz, DMSO, 25 °C, TMS) δ = 13.65 (s, 1H), 8.32−8.29 (m, 2H), 7.83−7.80 (m, 2H), 7.58−7.55 (m, 2H), 7.50−7.46 (m, 3H), 7.27 ppm (s, 1H); ^{13}C NMR (100 MHz, DMSO, 25 °C, TMS) δ = 164.0, 147.5, 132.9, 131.5, 129.7, 129.0, 127.9, 127.3, 125.1, 124.1, 121.5, 101.2, 99.4, 91.2, 85.1; HRMS (EI) m/z [M]$^+$calcd for $C_{19}H_{11}NO_4$ 317.0688, found 317.0688.

*(E)-5-(Naphthalen-1-yl)-2-(phenylethynyl)pent-2-en-4-ynoic Acid (**1k**).* Prepared according to procedure A in 62% yield over two steps (199.9 mg): ^{1}H NMR (400 MHz, DMSO, 25 °C, TMS) δ = 13.55 (s, 1H), 8.38 (d, J = 7.6 Hz, 1H), 8.10−8.01 (m, 2H), 7.89 (d, J = 5.2 Hz, 1H), 7.61−7.42 (m, 8H), 7.16 ppm (s, 1H); ^{13}C NMR (100 MHz, DMSO, 25 °C, TMS) δ = 164.4, 132.7, 132.3, 131.9, 131.7, 130.7, 129.5, 128.8, 128.7, 127.5, 126.9, 126.5, 125.8, 125.2, 125.1, 121.7, 118.7, 102.2, 98.4, 92.3, 85.4; HRMS (EI) m/z [M]$^+$ calcd for $C_{23}H_{14}O_2$ 322.0994, found 322.0986.

*(E)-5-Phenyl-2-(p-tolylethynyl)pent-2-en-4-ynoic Acid (**1l**).* Prepared according to procedure A in 78% yield over two steps (223.3 mg): ^{1}H NMR (400 MHz, DMSO, 25 °C, TMS) δ = 13.46 (s, 1H), 7.57−7.55 (m, 2H), 7.50−7.46 (m, 3H), 7.45 (d, J = 8.0 Hz, 2H), 7.29 (d, J = 8.4 Hz, 2H), 7.20 (s, 1H), 2.35 ppm (s, 3H); ^{13}C NMR (100 MHz, DMSO, 25 °C, TMS) δ = 164.4, 139.5, 131.7, 131.3, 130.1, 129.6, 129.1, 125.8, 125.7, 121.4, 118.7, 104.1, 98.8, 87.4, 84.8, 21.1; HRMS (EI) m/z[M]$^+$ calcd for $C_{20}H_{14}O_2$ 286.0994, found 286.0988.

*(E)-2-(Hex-1-yn-1-yl)dec-2-en-4-ynoic Acid (**1m**).* Prepared according to procedure A in 51% yield over two steps (125.6 mg); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 10.02 (s, 1H), 6.91−6.90 (m, 1H), 2.43−2.38 (m, 4H), 1.57−1.24 (m, 10H), 0.88−0.82 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 170.1, 129.3, 123.6, 108.8, 100.3, 78.7, 75.1, 31.0, 30.5, 28.1, 22.2, 21.9, 20.3, 19.5, 14.0, 13.6; HRMS (EI) m/z [M]$^+$ calcd for $C_{16}H_{22}O_2$ 246.1620, found 246.1619.

*(E)-Ethyl 5-Phenyl-2-(phenylethynyl)pent-2-en-4-ynoate (**2a**).* Prepared according to procedure C in 85% yield (510.6 mg): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 7.49−7.43 (m, 4H), 7.28−7.24 (m, 6H), 7.11 (s, 1H), 4.23−4.20 (m, 2H), 1.28 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 164.1, 132.2, 131.9, 129.6, 129.0, 128.6, 128.5, 126.8, 124.7, 122.8, 122.5, 105.3, 99.3, 87.5, 84.7, 61.9, 14.3; HRMS (EI) m/z [M]$^+$ calcd for $C_{21}H_{16}O_2$ 300.1150, found 300.1143.

*(E)-Ethyl 2-(Phenylethynyl)dec-2-en-4-ynoate (**2b**).* Prepared according to procedure D in 62% yield over two steps (365.0 mg): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 7.45−7.43 (m, 2H), 7.26−7.25 (m, 3H), 6.92−6.91 (m, 1H), 4.24−4.18 (m, 2H), 2.45−2.41 (m, 2H), 1.55−1.50 (m, 2H), 1.38−1.32 (m, 2H), 1.31−1.20 (m, 5H), 0.78 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 164.4, 131.9, 128.7, 128.3, 128.1, 124.1, 122.9, 108.5, 97.9, 84.4, 78.8, 61.8, 31.0, 28.2, 22.2, 20.4, 14.2, 13.9; HRMS (EI) m/z [M]$^+$ calcd for $C_{20}H_{22}O_2$ 294.1620, found 294.1619.

*(E)-Ethyl 5-(4-Iodophenyl)-2-(phenylethynyl)pent-2-en-4-ynoate (**2c**).* Prepared according to the typical procedure B in 85% yield over two steps (362.3 mg); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 7.63−7.61 (m, 2H), 7.48−7.46 (m, 2H), 7.30−7.28 (m, 3H), 7.17−7.15 (m, 2H), 7.08 (s, 1H), 4.28−4.22 (m, 2H), 1.30 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 164.0, 137.8, 133.4, 131.8, 129.1, 128.5, 126.3, 125.2, 122.7, 121.9, 103.9, 99.5, 96.0, 88.7, 84.6, 62.0, 14.2; HRMS (EI) m/z [M]$^+$ calcd for $C_{21}H_{15}IO_2$ 426.0117, found 426.0114.

*(E)-Methyl 5-Phenyl-2-(phenylethynyl)pent-2-en-4-ynoate (**2d**).* Prepared according to procedure C in 75% yield (429.5 mg): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 7.49−7.42 (m, 4H), 7.28−7.23 (m, 6H), 7.12 (s, 1H), 3.77 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 163.6, 131.1, 130.8, 128.6, 128.0, 127.5, 127.4, 126.1, 123.2, 121.7, 121.4, 104.4, 98.2, 86.4, 83.5, 51.8; HRMS (EI) m/z [M]$^+$calcd for $C_{20}H_{14}O_2$ 286.0994, found 286.0995.

*(E)-Ethyl 5-(p-Tolyl)-2-(p-tolylethynyl)pent-2-en-4-ynoate (**2e**).* Prepared according to procedure C in 77% yield (505.7 mg): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 7.39−7.33 (m, 4H), 7.09−7.06 (m, 5H), 4.26−4.20 (m, 2H), 2.29 (s, 6H), 1.29 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 164.3, 140.0, 139.2, 132.1, 131.8, 129.4, 129.2, 126.6, 124.3, 119.8, 119.5, 105.7, 99.4, 87.3, 84.3, 61.9, 21.7, 21.6, 14.3; HRMS (EI) m/z [M]$^+$ calcd for $C_{23}H_{20}O_2$ 328.1463, found 328.1468.

*(E)-Ethyl 5-(4-(Trifluoromethyl)phenyl)-2-((4-(trifluoromethyl)-phenyl)ethynyl)pent-2-en-4-ynoate (**2f**).* Prepared according to procedure C in 59% yield (514.9 mg): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 7.60−7.55 (m, 8H), 7.17 (s, 1H), 4.31−4.26 (m, 2H), 1.32 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 163.5, 132.2, 132.0, 131.4 (q, J = 24.2 Hz), 127.0, 126.3 (q, J = 18.6 Hz), 125.6, 125.5, 125.5, 125.5, 125.4, 125.4, 125.2 (q, J = 135.2 Hz), 103.4, 97.8, 88.8, 86.4, 62.2, 14.2; HRMS (EI) m/z [M]$^+$ calcd for $C_{23}H_{14}F_6O_2$ 436.0898, found 436.0899.

DOI: 10.1021/acs.joc.5b02870
J. Org. Chem. 2016, 81, 2770−2781

*(E)-Ethyl 5-(4-Chlorophenyl)-2-((4-chlorophenyl)ethynyl)pent-2-en-4-ynoate (**2g**).* Prepared according to procedure C in 63% yield (465.2 mg): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 7.41−7.34 (m, 4H), 7.34−7.25 (m, 4H), 7.11 (s, 1H), 4.28−4.22 (m, 2H), 1.30 ppm (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 163.8, 135.9, 135.2, 133.2, 133.0, 129.0, 128.9, 126.7, 124.8, 121.2, 120.8, 104.0, 98.1, 88.2, 85.5, 62.1, 14.2; HRMS (EI) m/z $[M]^+$ calcd for $C_{21}H_{14}Cl_2O_2$ 368.0371, found 368.0377.

*(E)-Ethyl 5-(4-Nitrophenyl)-2-((4-nitrophenyl)ethynyl)pent-2-en-4-ynoate (**2h**).* Prepared according to procedure C in 55% yield (429.4 mg): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.18 (d, J = 8.0 Hz, 4H), 7.63−7.58 (m, 4H), 7.20 (s, 1H), 4.31−4.26 (m, 2H), 1.33 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 163.1, 147.9, 147.6, 132.8, 132.5, 129.1, 128.7, 127.1, 125.8, 123.9, 123.8, 102.7, 97.5, 90.9, 88.8, 62.5, 12.2; HRMS (EI) m/z $[M]^+$ calcd for $C_{21}H_{14}N_2O_6$ 390.0852, found 390.0853.

*(E)-Methyl 5-Cyclopropyl-2-(phenylethynyl)pent-2-en-4-ynoate (**2i**).* Prepared according to procedure E in 55% yield (275.3 mg): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 7.46−7.43 (m, 2H), 7.28−7.27 (m, 3H), 6.90 (d, J = 6.4 Hz, 1H), 3.76 (s, 3H), 1.51−1.44 (m, 1H), 0.94−0.87 (m, 2H), 0.86−0.80 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 163.7, 130.5, 127.5, 127.2, 127.1, 121.8, 121.5, 111.3, 96.5, 83.1, 73.3, 51.5, 8.8, 0.014; HRMS (EI) m/z $[M]^+$calcd for $C_{17}H_{14}O_2$ 250.0994, found 250.0991.

*(E)-Ethyl 2-((4-Methoxyphenyl)ethynyl)dec-2-en-4-ynoate (**2j**).* Prepared according to procedure D in 62% yield over two steps (402.3 mg): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 7.40−7.36 (m, 2H), 6.88−6.86 (m, 1H), 6.80−6.77 (m, 2H), 4.24−4.18 (m, 2H), 3.75 (s, 3H), 2.45−2.41 (m, 2H), 1.58−1.50 (m, 2H), 1.39−1.35 (m, 2H), 1.33−1.21 (m, 5H), 0.79 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 163.3, 159.0, 132.4, 126.1, 123.2, 114.0, 112.9, 106.9, 97.1, 82.4, 77.8, 60.7, 54.3, 30.0, 27.2, 21.2, 19.3, 13.2, 12.9; HRMS (EI) m/z $[M]^+$ calcd for $C_{21}H_{24}O_3$ 324.1725, found 324.1730.

*(E)-Ethyl 5-(4-Methoxyphenyl)-2-(phenylethynyl)pent-2-en-4-ynoate (**2k**).* Prepared according to procedure B in 55% yield (181.7 mg): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 7.47−7.36 (m, 4H), 7.31−7.26 (m, 3H), 7.08 (s, 1H), 6.82−6.79 (m, 2H), 4.27−4.22 (m, 2H), 3.76 (s, 3H), 1.30 ppm (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 164.3, 160.2, 133.4, 132.1, 129.5, 128.6, 125.7, 124.9, 122.6, 114.9, 114.1, 104.8, 99.6, 87.6, 83.8, 61.9, 55.4, 14.2; HRMS (EI) m/z $[M]^+$ calcd for $C_{22}H_{18}O_3$ 330.1256, found 330.1255.

*(E)-Methyl 5-(4-Nitrophenyl)-2-(phenylethynyl)pent-2-en-4-ynoate (**2l**).* Prepared according to procedure E in 55% yield (364.5 mg): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.16−8.14 (m, 2H), 7.60−7.58 (m, 2H), 7.50−7.47 (m, 2H), 7.32−7.30 (m, 3H), 7.12 (s, 1H), 3.83 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 163.1, 146.7, 131.7, 130.8, 129.7, 128.4, 128.0, 127.5, 125.3, 124.5, 122.8, 122.5, 121.3, 100.7, 99.4, 90.5, 83.2, 52.1; HRMS (EI) m/z $[M]^+$ calcd for $C_{20}H_{13}NO_4$ 331.0845, found 331.0840.

General Procedure for the Synthesis of 3. A dry 10 mL round flask was charged with a solution of acid **1** (0.2 mmol), $PdCl_2$ (1.8 mg, 0.01 mmol), and $CuBr_2$ (26.8 mg, 0.12 mmol) in DMF (2.0 mL) under oxygen atmosphere at 60 °C. The reaction was monitored by TLC and stopped until the complete consumption of acid **1**. The solvent was concentrated under vacuum, saturated NH_4Cl (10 mL) was added, and the resulting mixture was extracted with EtOAc (3 × 5 mL). The combined organic layers were dried over Na_2SO_4, filtrated, and evaporated. The crude product was purified by silica gel chromatography using n-hexane/EtOAc = 1:1 as the eluent to give the product **3**. For **3d**, **3e**, and **3f**, the corresponding esters **3d′**, **3e′**, and **3f′** were isolated as the products after treatment with 2.0 equiv of CH_3I and K_2CO_3 in DMF.

*3,7-Dibenzoyl-4,8-diphenylnaphthalene-2,6-dicarboxylic Acid (**3a**).* A mixture of $PdCl_2$ (1.8 mg, 0.01 mmol), $CuBr_2$ (26.8 mg, 0.12 mmol), and (*E*)-5-phenyl-2-(phenylethynyl)pent-2-en-4-ynoic acid (**1a**) (54.5 mg, 0.2 mmol) in DMF (2.0 mL) was stirred under oxygen atmosphere at 60 °C for 3.5 h. The crude product was purified by column chromatography on silica gel (n-hexane/EtOAc = 1:1, v/v) to afford **3a** (47.3 mg, 82%): ^{1}H NMR (400 MHz, DMSO, 25 °C, TMS) δ = 13.39 (s, 2H), 8.20 (s, 2H), 7.51−7.47 (m, 6H), 7.36−7.33 (m, 10H), 7.22 ppm (s, 4H); ^{13}C NMR (100 MHz, DMSO, 25 °C, TMS) δ = 195.6, 166.4, 139.1, 137.9, 137.6, 135.2, 132.9, 132.7, 130.7, 129.5, 128.9, 128.5, 128.2, 128.1, 127.9; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{38}H_{25}O_6$ 577.1646, found 577.1649.

*Dimethyl 3,7-Bis(4-bromobenzoyl)-4,8-bis(4-bromophenyl)-naphthalene-2,6-dicarboxylate (**3d′**).* A mixture of $PdCl_2$ (1.8 mg, 0.01 mmol), $CuBr_2$ (26.8 mg, 0.12 mmol), and (*E*)-5-(4-bromophenyl)-2-((4-bromophenyl)ethynyl)pent-2-en-4-ynoic acid (**1d**) (86.0 mg, 0.2 mmol) in DMF (2.0 mL) was stirred under oxygen atmosphere at 60 °C for 8 h. To the mixture were added K_2CO_3 (55.2 mg, 0.4 mmol) and MeI (56.8 mg, 0.4 mmol). The reaction was stirred at 40 °C for 12 h. Thereafter, the resulting mixture was filtered through Celite, and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (n-hexane/EtOAc = 5:1, v/v) to afford **3d′** (66.3 mg, 72%): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.24 (s, 2H), 7.41−7.34 (m, 12H), 7.04−6.93 (m, 4H), 3.61 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 195.3, 165.6, 138.7, 138.3, 136.4, 133.7, 133.4, 132.4, 131.7, 131.5, 130.1, 129.7, 128.9, 128.3, 123.1, 52.9; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{40}H_{25}Br_4O_6$ 916.8379, found 916.8372.

*Dimethyl 3,7-Bis(4-methylbenzoyl)-4,8-di-p-tolylnaphthalene-2,6-dicarboxylate (**3e′**).* A mixture of $PdCl_2$ (1.8 mg, 0.01 mmol), $CuBr_2$ (26.8 mg, 0.12 mmol), and (*E*)-5-(*p*-tolyl)-2-(*p*-tolylethynyl)-pent-2-en-4-ynoic acid (**1e**) (60.1 mg, 0.2 mmol) in DMF (2.0 mL) was stirred under oxygen atmosphere at 60 °C for 8 h. To the mixture were added K_2CO_3 (55.2 mg, 0.4 mmol) and MeI (56.8 mg, 0.4 mmol). The reaction was stirred at 40 °C for 12 h. Thereafter, the resulting mixture was filtered through Celite, and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (n-hexane/EtOAc = 5:1, v/v) to afford **3e′** (44.2 mg, 67%): ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.28 (s, 2H), 7.41 (d, J = 7.8 Hz, 4H), 7.07−6.97 (m, 12H), 3.52 (s, 6H), 2.27 (s, 6H), 2.25 ppm (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C, TMS) δ = 196.6, 166.3, 143.5, 140.1, 138.4, 137.9, 135.7, 133.9, 132.4, 130.8, 129.8, 129.1, 129.0, 128.9, 128.8, 52.6, 21.8, 21.4; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{44}H_{37}O_6$ 661.2585, found 661.2579.

*Dimethyl 3,7-Bis(4-(trifluoromethyl)benzoyl)-4,8-bis(4-(trifluoromethyl)phenyl)naphthalene-2,6-dicarboxylate (**3f′**).* A mixture of (*E*)-5-(4-(trifluoromethyl)phenyl)-2-((4-(trifluoromethyl)-phenyl)ethynyl)pent-2-en-4-ynoic acid (**1f**) (81.7 mg, 0.2 mmol), $PdCl_2$ (1.8 mg, 0.01 mmol), and $CuBr_2$ (26.8 mg, 0.12 mmol) was stirred in DMF (2.0 mL) under oxygen atmosphere at 60 °C for 8 h. To the mixture were added K_2CO_3 (55.2 mg, 0.4 mmol) and MeI (56.8 mg, 0.4 mmol). The reaction was stirred at 40 °C for 12 h. Thereafter, the resulting mixture was filtered through Celite, and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (n-hexane/EtOAc = 5:1, v/v) to afford **3f′** (64.5 mg, 74%): ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.30 (s, 2H), 7.62−7.54 (m, 12H), 7.32 (d, J = 6.6 Hz, 4H), 3.67 ppm (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 197.7, 168.1, 142.8, 141.3, 141.2, 141.1, 137.2 (q, J = 64.5 Hz), 135.8, 133.9, 133.9 (q, J = 61.5 Hz), 132.4, 131.9, 131.5, 128.1 (q, J = 7.5 Hz), 128.0 (d, J = 9.0 Hz), 127.2 (q, J = 271.5 Hz), 55.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{44}H_{25}F_{12}O_6$ 877.1454, found 877.1467.

*3,7-Bis(4-methylbenzoyl)-4,8-dipentylnaphthalene-2,6-dicarboxylic Acid (**3g**).* A mixture of $PdCl_2$ (1.8 mg, 0.01 mmol), $CuBr_2$ (26.8 mg, 0.12 mmol), and (*E*)-2-(*p*-tolylethynyl)dec-2-en-4-ynoic acid (**1g**) (56.1 mg, 0.2 mmol) in DMF (2.0 mL) was stirred under oxygen atmosphere at 60 °C for 3.5 h. The crude product was purified by column chromatography on silica gel (n-hexane/EtOAc = 2:1, v/v) to afford **3g** (46.8 mg, 79%): ^{1}H NMR (400 MHz, DMSO, 25 °C, TMS) δ = 13.43 (s, 2H), 8.73 (s, 2H), 7.62 (d, J = 7.6 Hz, 4H), 7.33 (d, J = 7.6 Hz, 4H), 3.11−2.91 (m, 2H), 2.84−2.63 (m, 2H), 2.38 (s, 6H), 1.70−1.48 (m, 4H), 1.34−1.18 (m, 8H), 0.78 ppm (t, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, DMSO, 25 °C, TMS) δ = 196.4, 166.6, 143.6, 138.5, 137.4, 135.4, 132.5, 129.3, 129.1, 128.6, 125.9, 31.3, 30.5, 29.4,

DOI: 10.1021/acs.joc.5b02870
J. Org. Chem. 2016, 81, 2770−2781

21.4, 21.2, 13.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{38}H_{41}O_6$ 593.2898, found 593.2893.

*4,8-Bis(benzo[d][1,3]dioxol-5-yl)-3,7-dibenzoylnaphthalene-2,6-dicarboxylic Acid (**3h**).* A mixture of $PdCl_2$ (1.8 mg, 0.01 mmol), $CuBr_2$ (26.8 mg, 0.12 mmol), and (*E*)-5-(benzo[*d*][1,3]dioxol-5-yl)-2-(phenylethynyl)pent-2-en-4-ynoic acid (**1h**) (63.3 mg, 0.2 mmol) in DMF (2.0 mL) was stirred under oxygen atmosphere at 60 °C for 7 h. The crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 1:1, v/v) to afford **3h** (47.2 mg, 71%): ^{1}H NMR (400 MHz, DMSO, 25 °C, TMS) δ = 13.42 (s, 2H), 8.26 (s, 2H), 7.54−7.50 (m, 6H), 7.39−7.36 (m, 4H), 6.87−6.63 (m, 6H), 6.06 (s, 2H), 6.01 ppm (m, 2H); ^{13}C NMR (100 MHz, DMSO, 25 °C, TMS) δ = 195.7, 166.4, 146.9, 146.7, 138.7, 138.2, 137.7, 133.2, 132.7, 129.5, 128.8, 128.5, 128.3, 124.6, 111.2, 107.8, 101.2; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{40}H_{25}O_{10}$ 665.1442, found 665.1444.

General Procedure for the Synthesis of 4. A dry 10 mL round flask was charged with a solution of ester **2** (0.2 mmol), $PdCl_2$ (1.8 mg, 0.01 mmol), and $CuCl_2$ (5.4 mg, 0.04 mmol) in DMF (2.0 mL) under oxygen atmosphere at 60 °C. The reaction was monitored by TLC and stopped until the complete consumption of ester **2**. The solvent was concentrated under vacuum, saturated NH_4Cl (10 mL) was added, and the resulting mixture was extracted with DCM (3 × 5 mL). The combined organic layers were dried over Na_2SO_4, filtrated, and evaporated. The crude product was purified by silica gel chromatography using *n*-hexane/acetone as the eluent to give the ester product **4**. For **4c**, **4f**, and **4h**, the corresponding esters **4c′**, **4f′**, and **4h′** were isolated as the products after being treated with 2.0 equiv of CH_3I and K_2CO_3 in DMF.

*3,7-Dibenzoyl-6-(ethoxycarbonyl)-4,8-diphenyl-2-naphthoic Acid (**4a**).* A mixture of $PdCl_2$ (1.8 mg, 0.01 mmol), $CuCl_2$ (5.4 mg, 0.04 mmol), and (*E*)-ethyl-5-phenyl-2-(phenylethynyl)pent-2-en-4-ynoate (**2a**) (60.1 mg, 0.2 mmol) in DMF (2.0 mL) was stirred under oxygen atmosphere at 60 °C for 6 h. The crude product was purified by column chromatography on silica gel (*n*-hexane/acetone = 2:1, v/v) to afford **4a** (50.2 mg, 83%): ^{1}H NMR (400 MHz, DMSO, 25 °C, TMS) δ = 13.45 (s, 1H), 8.22 (s, 1H), 8.18 (s, 1H), 7.55−7.47 (m, 6H), 7.38−7.28 (m, 10H), 7.28−7.17 (m, 4H), 3.99−3.94 (m, 2H), 0.82 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO, 25 °C, TMS) δ = 195.6, 195.5, 166.3, 164.9, 139.3, 139.2, 138.1, 137.6, 137.4, 137.3, 135.1, 133.0, 132.9, 132.9, 132.7, 130.7, 129.7, 128.9, 128.7, 128.5, 128.3, 128.3, 128.3, 128.1, 127.9, 127.9, 61.5, 13.1; HRMS (EI) m/z $[M]^+$ calcd for $C_{40}H_{28}O_6$604.1886, found 604.1883.

*3,7-Dibenzoyl-6-(ethoxycarbonyl)-4,8-diphenyl-2-naphthoic Acid (**4b**).* A mixture of $PdCl_2$ (1.8 mg, 0.01 mmol), $CuCl_2$ (5.4 mg, 0.04 mmol), and (*E*)-ethyl-2-(phenylethynyl)dec-2-en-4-ynoate (**2b**) (58.9 mg, 0.2 mmol) in DMF (2.0 mL) under oxygen atmosphere at 60 °C for 10 h. The crude product was purified by column chromatography on silica gel (*n*-hexane/acetone = 4:1, v/v) to afford **4b** (42.7 mg, 72%): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.75 (s, 1H), 8.72 (s, 1H), 7.76 (d, J = 7.2 Hz, 2H), 7.69 (d, J = 5.6 Hz, 2H), 7.53−7.46 (m, 2H), 7.40−7.33 (m, 4H), 4.13−4.08 (m, 2H), 2.86 (s, 4H), 1.52 (s, 4H), 1.26−1.16 (s, 8H), 1.05 (t, J = 7.2 Hz, 3H), 0.77−0.73 ppm (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 196.5, 164.6, 138.9, 136.8, 136.2, 132.3, 128.0, 127.8, 127.8, 127.6, 127.5, 125.6, 60.8, 31.0, 31.0, 30.3, 30.1, 29.3, 28.7, 21.0, 12.8, 12.8, 12.6; HRMS (EI) m/z $[M]^+$ calcd for $C_{38}H_{40}O_6$ 592.2825, found 592.2829.

*2-Ethyl 6-Methyl 3,7-dibenzoyl-4,8-bis(4-iodophenyl)-naphthalene-2,6-dicarboxylate (**4c′**).* A mixture of $PdCl_2$ (1.8 mg, 0.01 mmol), $CuCl_2$ (5.4 mg, 0.04 mmol), and (*E*)-ethyl-5-(4-iodophenyl)-2-(phenylethynyl)pent-2-en-4-ynoate (**2c**) (85.2 mg, 0.2 mmol) in DMF (2.0 mL) was stirred under oxygen atmosphere at 60 °C for 8 h. To the mixture were added K_2CO_3 (55.2 mg, 0.4 mmol) and MeI (56.8 mg, 0.4 mmol). The reaction was stirred at 40 °C for 12 h. Thereafter, the resulting mixture was filtered through Celite, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (*n*-hexane/CH_2Cl_2 = 2:1, v/v) to afford **4c′** (47.0 mg, 54%): ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.31 (s, 1H), 8.29 (s, 1H), 7.62 (d, J = 6.0 Hz, 4H), 7.54 (d, J = 6.6 Hz, 4H), 7.46−7.44 (m, 2H), 7.31−7.28 (m, 4H), 6.97−6.85 (m, 4H), 4.08−4.04 (m, 2H), 3.62 (m, 3H), 0.95 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C, TMS) δ = 196.7, 196.5, 166.2, 165.7, 139.1, 139.0, 138.9, 138.7, 138.1, 138.1, 137.6, 137.6, 135.0, 135.0, 133.6, 133.5, 133.4, 133.3, 132.9, 130.1, 129.9, 129.6, 129.3, 129.2, 129.1, 128.6, 128.6, 95.0, 94.9, 62.3, 53.0, 13.8; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{41}H_{29}I_2O_6$ 871.0048, found 871.0039.

*3,7-Dibenzoyl-6-(methoxycarbonyl)-4,8-diphenyl-2-naphthoic Acid (**4d**).* A mixture of $PdCl_2$ (1.8 mg, 0.01 mmol), $CuCl_2$ (5.4 mg, 0.04 mmol), and (*E*)-methyl-5-phenyl-2-(phenylethynyl)pent-2-en-4-ynoate (**2d**) (57.3 mg, 0.2 mmol) in DMF (2.0 mL) under oxygen atmosphere at 60 °C for 8 h. The crude product was purified by column chromatography on silica gel (*n*-hexane/acetone = 2:1, v/v) to afford **4d** (43.7 mg, 74%): ^{1}H NMR (400 MHz, DMSO, 25 °C, TMS) δ = 13.45 (s, 1H), 8.22 (s, 1H), 8.20 (s, 1H), 7.54−7.47 (m, 6H), 7.37−7.24 (m, 10H), 7.23 (s, 4H), 3.53 ppm (s, 3H); ^{13}C NMR (100 MHz, DMSO, 25 °C, TMS) δ = 195.6, 195.5, 166.3, 165.3, 139.3, 139.1, 138.2, 138.2, 137.6, 137.3, 135.0, 133.0, 132.9, 132.8, 132.7, 132.7, 130.7, 128.9, 128.5, 128.3, 128.2, 127.9, 52.6; HRMS (EI) m/z $[M]^+$ calcd for $C_{39}H_{26}O_6$ 590.1729, found 590.1723.

*6-(Ethoxycarbonyl)-3,7-bis(4-methylbenzoyl)-4,8-di(p-tolyl)-2-naphthoic acid (**4e**).* A mixture of $PdCl_2$ (1.8 mg, 0.01 mmol), $CuCl_2$ (5.4 mg, 0.04 mmol), and (*E*)-ethyl-5-(*p*-tolyl)-2-(p-tolylethynyl)pent-2-en-4-ynoate (**2e**) (65.7 mg, 0.2 mmol) in DMF (2.0 mL) under oxygen atmosphere at 60 °C for 8 h. The crude product was purified by column chromatography on silica gel (*n*-hexane/acetone = 3:1, v/v) to afford **4e** (49.6 mg, 75%): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.29 (s, 1H), 8.25 (s, 1H), 7.40 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 7.6 Hz, 2H), 7.05−6.94 (m, 12H), 3.97−3.92 (m, 2H), 2.26−2.23 (m, 12H), 0.86 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 196.4, 196.3, 169.8, 165.8, 143.5, 143.4, 140.1, 140.0, 138.3, 138.1, 137.8, 137.8, 135.6, 135.5, 134.2, 133.6, 132.2, 132.1, 130.8, 130.7, 130.6, 129.7, 129.2, 129.1, 129.0, 128.9, 128.8, 128.7, 127.2, 61.7, 21.7, 21.3, 21.3, 13.4; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{44}H_{37}O_6$ 661.2585, found 661.2585.

*2-Ethyl 6-Methyl 3,7-bis(4-(trifluoromethyl)benzoyl)-4,8-bis(4-(trifluoromethyl)phenyl)naphthalene-2,6-dicarboxylate (**4f′**).* A mixture of (*E*)-ethyl-5-(4-(trifluoromethyl)phenyl)-2-((4-(trifluoromethyl) phenyl)ethynyl)pent-2-en-4-ynoate (**2f**) (87.3 mg, 0.2 mmol), $PdCl_2$ (1.8 mg, 0.01 mmol), and $CuCl_2$ (5.4 mg, 0.04 mmol) in DMF (2.0 mL) was stirred under oxygen atmosphere at 60 °C for 8 h. To the mixture were added K_2CO_3 (55.2 mg, 0.4 mmol) and MeI (56.8 mg, 0.4 mmol). The reaction was stirred at 40 °C for 12 h. Thereafter, the resulting mixture was filtered through Celite, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (*n*-hexane/CH_2Cl_2 = 2:1, v/v) to afford **4f′** (59.7 mg, 67%): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.24 (s, 1H), 8.23 (s, 1H), 7.58−7.48 (m, 12H), 7.27−7.25 (m, 4H), 4.07−4.01 (m, 2H), 3.61 (s, 3H), 0.93 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 195.2, 195.1, 165.5, 165.0, 140.3, 140.2, 1838.7, 138.6, 138.5, 138.5, 138.4, 138.3, 134.4 (q, J = 32.6 Hz), 133.3, 133.1, 131.3, 131.1 (q, J = 32.5 Hz), 129.9, 129.8, 129.5, 129.1, 129.0, 128.9, 125.5, 125.5, 125.4, 125.4, 125.3, 125.3, 125.3, 125.1 (q, J = 271.1 Hz), 62.4, 53.0, 13.5,; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{45}H_{27}F_{12}O_6$ 891.1611, found 891.1616..

*3,7-Bis(4-chlorobenzoyl)-4,8-bis(4-chlorophenyl)-6-(ethoxycarbonyl)-2-naphthoic Acid (**4g**).* A mixture of $PdCl_2$ (1.8 mg, 0.01 mmol), $CuCl_2$ (5.4 mg, 0.04 mmol), and (*E*)-ethyl 5-(4-chlorophenyl)-2-((4-chlorophenyl)ethynyl)pent-2-en-4-ynoate (**2g**) (73.8 mg, 0.2 mmol) in DMF (2.0 mL) was stirred under oxygen atmosphere at 60 °C for 8 h. The crude product was purified by column chromatography on silica gel (*n*-hexane/acetone = 3:1, v/v) to afford **4g** (45.2 mg, 61%): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.27 (s, 1H), 8.23 (s, 1H), 7.43 (d, J = 8.8 Hz, 2H), 7.34 (d, J = 6.8 Hz, 2H), 7.23−7.03 (m, 9H), 6.93 (s, 3H), 4.06−4.00 (m, 2H), 0.93 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 195.1, 169.1, 165.2, 138.8, 138.2, 136.1, 136.0, 134.9, 134.8, 133.9, 133.3, 133.1, 133.0, 132.1, 132.1, 130.2, 130.0, 129.8, 129.5, 128.7, 128.7, 128.5, 62.2, 13.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{40}H_{25}Cl_4O_6$ 741.0400, found 741.0410.

DOI: 10.1021/acs.joc.5b02870
J. Org. Chem. 2016, 81, 2770−2781

*2-Ethyl 6-Methyl 3,7-bis(4-nitrobenzoyl)-4,8-bis(4-nitrophenyl)-naphthalene-2,6-dicarboxylate (**4h′**).* A mixture of $PdCl_2$ (1.8 mg, 0.01 mmol), $CuCl_2$ (5.4 mg, 0.04 mmol), and (*E*)-ethyl-5-(4-nitrophenyl)-2-((4-nitrophenyl)ethynyl)pent-2-en-4-ynoate (**2h**) (78.1 mg, 0.2 mmol) in DMF (2.0 mL) was stirred under oxygen atmosphere at 60 °C for 10 h. To the mixture were added K_2CO_3 (55.2 mg, 0.4 mmol) and MeI (56.8 mg, 0.4 mmol). The reaction was stirred at 40 °C for 12 h. Thereafter, the resulting mixture was filtered through Celite, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (*n*-hexane/CH_2Cl_2 = 2:1, v/v) to afford **4h′** (51.9 mg, 65%): ^{1}H NMR (600 MHz, DMSO, 25 °C, TMS) δ = 8.36−8.31 (m, 6H), 8.27−8.23 (m, 6H), 7.88−7.87 (m, 3H), 7.65−7.63 (m, 3H), 4.09−4.05 (m, 2H), 3.63 (s, 3H), 0.93 ppm (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, DMSO, 25 °C, TMS) δ = 197.1, 197.1, 168.0, 167.5, 153.0, 153.0, 150.7, 144.5, 144.4, 144.4, 144.4, 141.1, 140.5, 140.3, 135.8, 135.7, 135.4, 133.0, 132.9, 131.9, 131.5, 127.0, 127.0, 126.5, 126.4, 65.3, 56.2, 16.4; HRMS (ESI) *m*/*z* $[M + H]^+$ calcd for $C_{41}H_{27}N_4O_{14}$ 799.1518, found 799.1512.

General Procedure for the Synthesis of 5. A dry 10 mL round flask was charged with a solution of acid **1** (0.2 mmol), ester **2** (0.6 mmol), $PdCl_2$ (1.8 mg, 0.01 mmol), and CuI (38.1 mg, 0.2 mmol) in DMF (2.0 mL). The reaction mixture was stirred under O_2 at 60 °C and detected by TLC. After the complete consumption of **1**, saturated NH_4Cl (10 mL) was added, and the resulting mixture was extracted with DCM (3 × 5 mL). The combined organic layers were dried over Na_2SO_4, filtrated, and evaporated. The crude product was purified by silica gel chromatography using *n*-hexane/acetone as the eluent to give the ester product **5**.

*3,7-Dibenzoyl-6-(ethoxycarbonyl)-4-pentyl-8-phenyl-2-naphthoic Acid (**5ab**).* A mixture of acid **1a** (54.5 mg, 0.2 mmol), ester **2b** (176.6 mg, 0.6 mmol), $PdCl_2$ (1.8 mg, 0.01 mmol), and CuI (38.1 mg, 0.2 mmol) in DMF (2.0 mL) was stirred at 60 °C under O_2 for 0.75 h. The crude product was purified by column chromatography on silica gel (*n*-hexane/acetone = 4:1, v/v) to afford **5ab** (110.2 mg, 92%) and **2b** (106.0 mg, 0.36 mmol): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.84 (s, 1H), 8.12 (s, 1H), 7.61 (d, *J* = 6.8 Hz, 2H), 7.49−7.47 (m, 2H), 7.44−7.41 (m, 1H), 7.36−7.27 (m, 3H), 7.21−7.17 (m, 5H), 7.03 (s, 2H), 4.15−4.10 (m, 2H), 2.88 (s, 2H), 1.55 (s, 2H), 1.23−1.18 (m, 4H), 1.02 (t, *J* = 6.8 Hz, 3H), 0.76 ppm (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 196.8, 169.8, 165.7, 140.7, 139.1, 138.0, 137.9, 137.8, 135.2, 133.5, 132.8, 130.8, 129.8, 129.0, 129.0, 128.6, 128.2, 128.1, 128.0, 127.7, 127.2, 62.0, 32.1, 31.2, 30.1, 22.1, 13.9, 13.6; HRMS (ESI) *m*/*z* $[M + H]^+$ calcd for $C_{39}H_{35}O_6$ 599.2428, found 599.2429.

Gram-Scale Entry. Each entry was conducted by using **1a** (1.36 g, 5 mmol), **2b** (4.42 g, 15 mmol), $PdCl_2$ (44.3 mg, 0.25 mmol), and CuI (190.1 mg, 1 mmol) in DMF (25 mL) under O_2 at 60 °C. The reaction was stirred for 1 h, saturated NH_4Cl (10 mL) was added, and the resulting mixture was extracted with DCM (3 × 5 mL). The combined organic layers were dried over Na_2SO_4, filtrated, and evaporated. The crude product was purified by silica gel chromatography using *n*-hexane/acetone = 4:1 as the eluent to give the product **5ab** (2.66 g, 89%) and **2b** (3.12 g, 10.6 mmol).

*3,7-Dibenzoyl-6-(ethoxycarbonyl)-8-(4-methoxyphenyl)-4-pentyl-2-naphthoic Acid (**5cb**).* A mixture of acid **1c** (60.5 mg, 0.2 mmol), ester **2b** (176.6 mg, 0.6 mmol), $PdCl_2$ (1.8 mg, 0.01 mmol), and CuI (38.1 mg, 0.2 mmol) in DMF (2.0 mL) was stirred at 60 °C under O_2 for 1 h. The crude product was purified by column chromatography on silica gel (*n*-hexane/acetone = 3:1, v/v) to afford **5cb** (78.0 mg, 62%) and **2b** (117.8 mg, 0.4 mmol): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.82 (s, 1H), 8.17 (s, 1H), 7.62 (d, *J* = 7.2 Hz, 2H), 7.50−7.48 (m, 2H), 7.45−7.41 (m, 1H), 7.37−7.27 (m, 3H), 7.22−7.18 (m, 2H), 6.94 (d, *J* = 14.8 Hz, 2H), 6.70 (d, *J* = 7.2 Hz, 2H), 4.15−4.09 (m, 2H), 3.70 (s, 3H), 2.88 (s, 2H), 1.54 (s, 2H), 1.31−1.14 (m, 4H), 1.02 (t, *J* = 6.8 Hz, 3H), 0.76 ppm (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 195.9, 164.7, 158.2, 139.5, 138.0, 137.2, 136.8, 136.7, 133.3, 132.5, 131.7, 131.0, 127.9, 127.9, 127.5, 127.1, 126.4, 126.2, 112.5, 60.9, 54.1, 31.1, 30.1, 29.0, 21.1, 12.9, 12.6; HRMS (ESI) *m*/*z* $[M + H]^+$ calcd for $C_{40}H_{37}O_7$ 629.2534, found 629.2537..

*7-Benzoyl-3-(4-bromobenzoyl)-8-(4-bromophenyl)-6-(ethoxycarbonyl)-4-pentyl-2-naphthoic Acid (**5db**).* A mixture of acid **1d** (86.0 mg, 0.2 mmol), ester **2b** (176.6 mg, 0.6 mmol), $PdCl_2$ (1.8 mg, 0.01 mmol), and CuI (38.1 mg, 0.2 mmol) in DMF (2.0 mL) was stirred at 60 °C under O_2 for 1 h. The crude product was purified by column chromatography on silica gel (*n*-hexane/acetone = 3:1, v/v) to afford **5db** (122.5 mg, 81%) and **2b** (106.0 mg, 0.36 mmol): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.86 (s, 1H), 8.10 (s, 1H), 7.49−7.48 (m, 6H), 7.40−7.37 (m, 1H), 7.32−7.31 (m, 2H), 7.25−7.21 (m, 2H), 6.92 (s, 2H), 4.15−4.10 (m, 2H), 2.98−2.75 (m, 2H), 1.68−1.40 (m, 2H), 1.34−1.12 (m, 4H), 1.02 (t, *J* = 7.2 Hz, 3H), 0.78 ppm (t, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 195.5, 164.4, 138.3, 137.2, 136.7, 135.6, 133.0, 132.4, 132.0, 131.3, 130.9, 130.3, 129.2, 128.0, 127.9, 127.3, 126.9, 121.8, 61.1, 31.0, 30.1, 29.1, 21.0, 12.9, 12.6; HRMS (ESI) *m*/*z* $[M + H]^+$ calcd for $C_{39}H_{33}Br_2O_6$755.0638, found 755.0643.

*3,7-Dibenzoyl-6-(ethoxycarbonyl)-8-(4-nitrophenyl)-4-pentyl-2-naphthoic Acid (**5ib**).* A mixture of acid **1i** (63.5 mg, 0.2 mmol), ester **2b** (176.6 mg, 0.6 mmol), $PdCl_2$ (1.8 mg, 0.01 mmol), and CuI (38.1 mg, 0.2 mmol) in DMF (2.0 mL) was stirred at 60 °C under O_2 for 1 h. The crude product was purified by column chromatography on silica gel (*n*-hexane/acetone = 3:1, v/v) to afford **5ib** (100.4 mg, 78%) and **2b** (117.8 mg, 0.4 mmol): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.91 (s, 1H), 8.06 (d, *J* = 8.0 Hz, 2H), 7.96 (s, 1H), 7.62 (d, *J* = 6.0 Hz, 2H), 7.49−7.38 (m, 4H), 7.33−7.22 (m, 6H), 4.16−4.11 (m, 2H), 2.88 (s, 2H), 1.54 (s, 2H), 1.30−1.18 (m, 4H), 1.03 (t, *J* = 7.2 Hz, 3H), 0.77 ppm (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 196.1, 165.3, 147.6, 142.4, 139.6, 138.2, 138.1, 137.6, 133.4, 133.0, 131.9, 129.0, 128.9, 128.7, 128.5, 123.2, 62.3, 32.1, 31.2, 30.1, 22.1, 13.9, 13.6; HRMS (ESI) *m*/*z* $[M + H]^+$ calcd for $C_{39}H_{34}NO_8$ 644.2279, found 644.2286.

*3,7-Dibenzoyl-6-(ethoxycarbonyl)-4-pentyl-8-(thiophene-2-yl)-2-naphthoic Acid (**5jb**).* A mixture of **1j** (55.7 mg, 0.2 mmol), ester **2b** (176.6 mg, 0.6 mmol), $PdCl_2$ (1.8 mg, 0.01 mmol), and CuI (38.1 mg, 0.2 mmol) in DMF (2.0 mL) was stirred at 60 °C under O_2 for 1 h. The crude product was purified by column chromatography on silica gel (*n*-hexane/acetone = 3:1, v/v) to afford **5jb** (73.8 mg, 61%) and **2b** (117.8 mg, 0.4 mmol): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.87 (s, 1H), 8.42 (s, 1H), 7.66 (d, *J* = 6.0 Hz, 2H), 7.57 (d, *J* = 7.2 Hz, 2H), 7.46−7.23 (m, 7H), 6.86−6.82 (m, 2H), 4.17−4.11 (m, 2H), 3.07−2.69 (m, 2H), 1.55 (s, 2H), 1.23−1.14 (m, 4H), 1.03 (t, *J* = 6.8 Hz, 3H), 0.77 ppm (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 196.5, 165.5, 163.2, 139.8, 139.0, 137.9, 137.5, 134.8, 133.3, 132.9, 129.0, 128.8, 128.7, 128.6, 128.2, 128.0, 126.8, 62.1, 32.1, 31.1, 29.7, 22.1, 13.9, 13.6; HRMS (ESI) *m*/*z* $[M + H]^+$ calcd for $C_{37}H_{33}O_6S$ 605.1992, found 605.1989.

*2,6-Dibenzoyl-3-(ethoxycarbonyl)-5-pentyl[1,1′-binaphthalene]-7-carboxylic Acid (**5kb**).* A mixture of acid **1k** (64.5 mg, 0.2 mmol), ester **2b** (176.6 mg, 0.6 mmol), $PdCl_2$ (1.8 mg, 0.01 mmol), and CuI (38.1 mg, 0.2 mmol) in DMF (2.0 mL) was stirred at 60 °C under O_2 for 1 h. The crude product was purified by column chromatography on silica gel (*n*-hexane/acetone = 3:1, v/v) to afford **5kb** (114.2 mg, 88%) and **2b** (100.1 mg, 0.34 mmol): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.91 (s, 1H), 7.77 (s, 1H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.55 (d, *J* = 6.8 Hz, 2H), 7.38−7.20 (m, 7H), 7.17−7.12 (m, 2H), 7.07−6.98 (m, 4H), 4.14−4.08 (m, 2H), 2.88 (m, 2H), 1.58 (s, 2H), 1.33−1.17 (m, 4H), 0.98 (t, *J* = 7.2 Hz, 3H), 0.77 ppm (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 196.5, 169.5, 165.8, 139.2, 139.1, 137.7, 137.3, 134.4, 133.4, 133.0, 132.5, 132.5, 132.4, 129.6, 129.4, 129.1, 128.8, 128.7, 128.5, 128.2, 128.1, 127.8, 126.3, 126.3, 126.0, 124.7, 62.1, 32.2, 31.2, 30.2, 22.1, 13.9, 13.6; HRMS (ESI) *m*/*z* $[M + H]^+$ calcd for $C_{43}H_{37}O_6$ 649.2585, found 649.2582.

*7-Benzoyl-6-(ethoxycarbonyl)-3-(4-methylbenzoyl)-4-pentyl-8-phenyl-2-naphthoic Acid (**5 lb**).* A mixture of acid **1l** (57.3 mg, 0.2 mmol), ester **2b** (176.6 mg, 0.6 mmol), $PdCl_2$ (1.8 mg, 0.01 mmol), and CuI (38.1 mg, 0.2 mmol) in DMF (2.0 mL) was stirred at 60 °C under O_2 for 1 h. The crude product was purified by column chromatography on silica gel (*n*-hexane/acetone = 3:1, v/v) to afford

DOI: 10.1021/acs.joc.5b02870
J. Org. Chem. 2016, 81, 2770−2781

5lb (76.0 mg, 62%) and **2b** (111.8 mg, 0.38 mmol): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.84 (s, 1H), 8.14 (s, 1H), 7.52−7.48 (m, 4H), 7.36−7.32 (m, 1H), 7.21−7.18 (m, 5H), 7.10 (d, J = 8.0 Hz, 2H), 7.04 (s, 2H), 4.15−4.10 (m, 2H), 2.98−2.76 (m, 2H), 2.31 (s, 3H), 1.57 (s, 2H), 1.32−1.18 (m, 4H), 1.02 (t, J = 7.2 Hz, 3H), 0.77 ppm (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 196.8, 169.7, 165.8, 144.0, 140.6, 139.0, 137.9, 137.9, 135.4, 135.2, 133.8, 133.4, 132.8, 132.2, 130.8, 129.4, 129.3, 129.2, 129.0, 128.2, 128.1, 128.0, 127.7, 62.0, 32.1, 31.2, 30.1, 22.1, 21.8, 13.9, 13.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{40}H_{37}O_6$ 613.2585, found 613.2585.

*7-Benzoyl-6-(ethoxycarbonyl)-3-pentanoyl-4,8-dipentyl-2-naphthoic Acid (**5mb**).* A mixture of acid **1m** (86.0 mg, 0.2 mmol), ester **2b** (176.6 mg, 0.6 mmol), $PdCl_2$ (1.8 mg, 0.01 mmol), and CuI (38.1 mg, 0.2 mmol) in DMF (2.0 mL) was stirred at 60 °C under O_2 for 1 h. The crude product was purified by column chromatography on silica gel (n-hexane/acetone = 4:1, v/v) to afford **5mb** (66.4 mg, 58%) and **2b** (129.5 mg, 0.44 mmol): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.74 (s, 1H), 8.40 (s, 1H), 7.71 (d, J = 7.6 Hz, 2H), 7.51−7.47 (m, 1H), 7.38−7.34 (m, 2H), 4.56−4.36 (m, 1H), 4.18−4.08 (m, 2H), 3.35−3.15 (m, 2H), 2.78 (s, 2H), 2.37−2.15 (m, 2H), 1.77 (m, 1H), 1.60−1.50 (m, 3H), 1.45−1.38 (m, 3H), 1.27−1.09 (m, 8H), 1.04 (t, J = 7.2 Hz, 3H), 0.90 (t, J = 7.2 Hz, 3H), 0.78 (t, J = 6.8 Hz, 3H), 0.71 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 196.5, 167.2, 164.5, 139.1, 137.2, 136.7, 135.9, 133.8, 132.3, 128.0, 127.6, 127.5, 127.3, 125.9, 125.8, 120.2, 107.9, 60.9, 38.0, 31.4, 31.1, 30.4, 30.2, 29.6, 27.4, 24.7, 21.4, 21.3, 21.1, 13.0, 12.8, 12.8, 12.6; HRMS (EI) m/z $[M]^+$ calcd for $C_{36}H_{44}O_6$572.3138, found 572.3136.

*3-Benzoyl-6-(ethoxycarbonyl)-7-(4-methylbenzoyl)-8-phenyl-4-(p-tolyl)-2-naphthoic Acid (**5ae**).* A mixture of acid **1a** (54.5 mg, 0.2 mmol), ester **2e** (197.0 mg, 0.6 mmol), $PdCl_2$ (1.8 mg, 0.01 mmol), and CuI (38.1 mg, 0.2 mmol) in DMF (2.0 mL) was stirred at 60 °C under O_2 for 1 h. The crude product was purified by column chromatography on silica gel (n-hexane/acetone = 3:1, v/v) to afford **5ae** (68.3 mg, 54%) and **2e** (131.3 mg, 0.40 mmol): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.28 (s, 1H), 8.26 (s, 1H), 7.38 (d, J = 8.0 Hz, 4H), 7.31−7.28 (m, 2H), 7.20−7.04 (m, 6H), 6.99−6.92 (m, 6H), 3.99−3.93 (m, 2H), 2.25 (s, 3H), 2.23 (s, 3H), 0.86 ppm (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 195.7, 165.2, 143.0, 139.4, 137.7, 137.4, 137.4, 135.0, 134.7, 130.3, 130.2, 129.4, 128.8, 128.6, 128.4, 128.2, 127.7, 127.5, 127.5, 61.3, 21.2, 20.8, 12.9; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{42}H_{33}O_6$ 633.2272, found 633.2284.

*3-Benzoyl-6-(ethoxycarbonyl)-8-phenyl-7-(4-(trifluoromethyl)-benzoyl)-4-(4-(trifluoromethyl)phenyl)-2-naphthoic Acid (**5af**).* A mixture of acid **1a** (54.5 mg, 0.2 mmol), ester **2f** (261.8 mg, 0.6 mmol), $PdCl_2$ (1.8 mg, 0.01 mmol), and CuI (38.1 mg, 0.2 mmol) in DMF (2.0 mL) was stirred at 60 °C under O_2 for 1 h. The crude product was purified by column chromatography on silica gel (n-hexane/acetone = 3:1, v/v) to afford **5af** (87.4 mg, 59%) and **2f** (165.8 mg, 0.38 mmol): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.34 (s, 1H), 8.13 (s, 1H), 7.56 (d, J = 8.0 Hz, 2H), 7.45 (d, J = 8.4 Hz, 4H), 7.34−7.31 (m, 3H), 7.20−7.13 (m, 7H), 7.06 (d, J = 6.0 Hz, 2H), 4.04−3.99 (m, 2H), 0.90 ppm (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 194.6, 168.3, 164.3, 139.3, 139.2, 137.8, 136.8, 136.6, 133.4, 133.0, 132.7, 132.3, 132.0, 130.3, 129.8, 129.6, 129.3, 128.6, 128.3, 128.0, 127.6, 127.3, 127.2, 124.2, 124.1, 124.1, 124.0, 123.9, 123.8, 121.4, 121.1, 61.1, 12.4; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{42}H_{27}F_6O_6$ 741.1706, found 741.1713.

*3,7-Dibenzoyl-4-cyclopropyl-6-(methoxycarbonyl)-8-phenyl-2-naphthoic Acid (**5ai**).* A mixture of acid **1a** (54.5 mg, 0.2 mmol), ester **2i** (150.2 mg, 0.6 mmol), $PdCl_2$ (1.8 mg, 0.01 mmol), and CuI (38.1 mg, 0.2 mmol) in DMF (2.0 mL) was stirred at 60 °C under O_2 for 1 h. The crude product was purified by column chromatography on silica gel (n-hexane/acetone = 4:1, v/v) to afford **5ai** (103.5 mg, 91%) and **2i** (90.1 mg, 0.36 mmol): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 9.36 (s, 1H), 8.01 (s, 1H), 7.70 (d, J = 7.6 Hz, 2H), 7.49−7.42 (m, 3H), 7.36−7.29 (m, 3H), 7.21−7.16 (m, 5H), 7.08−6.97 (m, 2H), 3.69 (s, 3H), 1.97−1.90 (m, 1H), 1.06−0.35 ppm (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 197.0, 166.4, 140.3, 139.8, 138.3, 138.2, 137.8, 135.2, 135.1, 133.7, 133.0, 132.7, 130.8, 130.1, 128.9, 128.6, 128.5, 128.2, 128.2, 128.0, 52.7, 12.9, 9.1; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{36}H_{27}O_6$ 555.1802, found 555.1802.

*3-Benzoyl-6-(ethoxycarbonyl)-7-(4-methoxybenzoyl)-4-pentyl-8-phenyl-2-naphthoic Acid (**5aj**).* A mixture of **1a** (54.5 mg, 0.2 mmol), ester **2j** (194.6 mg, 0.6 mmol), $PdCl_2$ (1.8 mg, 0.01 mmol), and CuI (38.1 mg, 0.2 mmol) in DMF (2.0 mL) was stirred at 60 °C under O_2 for 1 h. The crude product was purified by column chromatography on silica gel (n-hexane/acetone = 3:1, v/v) to afford **5aj** (116.9 mg, 93%) and **2j** (110.3 mg, 0.34 mmol): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.83 (s, 1H), 8.12 (s, 1H), 7.61 (d, J = 7.6 Hz, 2H), 7.47 (d, J = 8.4 Hz, 2H), 7.45−7.40 (m, 1H), 7.31−7.27 (m, 2H), 7.24−6.92 (m, 5H), 6.69 (d, J = 8.8 Hz, 2H), 4.15−4.10 (m, 2H), 3.73 (s, 3H), 2.87 (s, 2H), 1.53 (s, 2H), 1.30−1.18 (m, 4H), 1.04 (t, J = 7.2 Hz, 3H), 0.76 ppm (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 197.0, 166.4, 140.3, 139.8, 138.3, 138.2, 137.8, 135.2, 135.1, 133.7, 133.0, 132.7, 130.8, 130.1, 128.9, 128.6, 128.5, 128.2, 128.2, 128.0, 52.7, 12.9, 9.1; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{40}H_{37}O_7$ 629.2534, found 629.2545.

*3,7-Dibenzoyl-6-(ethoxycarbonyl)-4-(4-methoxyphenyl)-8-phenyl-2-naphthoic Acid (**5ak**).* A mixture of acid **1a** (54.5 mg, 0.2 mmol), **2k** (198.2 mg, 0.6 mmol), $PdCl_2$ (1.8 mg, 0.01 mmol), and CuI (38.1 mg, 0.2 mmol) in DMF (2.0 mL) was stirred at 60 °C under O_2 for 1 h. The crude product was purified by column chromatography on silica gel (n-hexane/acetone = 3:1, v/v) to afford **5ak** (105.4 mg, 83%) and **2k** (112.3 mg, 0.34 mmol): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.29 (s, 1H), 8.24 (s, 1H), 7.46 (d, J = 8.8 Hz, 2H), 7.38 (d, J = 4.4 Hz, 2H), 7.31−7.27 (m, 2H), 7.20−7.04 (m, 11H), 6.68 (d, J = 8.8 Hz, 2H), 4.00−3.94 (m, 2H), 3.72 (s, 3H), 0.88 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 194.2, 164.6, 162.1, 138.8, 137.2, 136.8, 134.2, 134.0, 132.9, 130.2, 130.2, 129.8, 129.8, 129.8, 128.7, 128.3, 127.7, 127.3, 127.2, 127.1, 126.9, 126.9, 112.3, 60.7, 54.3, 12.4; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{41}H_{31}O_7$ 635.2064, found 635.2069.

*3,7-Dibenzoyl-6-(methoxycarbonyl)-4-(4-nitrophenyl)-8-phenyl-2-naphthoic Acid (**5al**).* A mixture of acid **1a** (54.5 mg, 0.2 mmol), ester **2l** (207.2 mg, 0.6 mmol), $PdCl_2$ (1.8 mg, 0.01 mmol), and CuI (38.1 mg, 0.2 mmol) in DMF (2.0 mL) was stirred at 60 °C under O_2 for 1 h. The crude product was purified by column chromatography on silica gel (n-hexane/acetone = 3:1, v/v) to afford **5al** (100.4 mg, 79%) and **2l** (124.3 mg, 0.36 mmol): ^{1}H NMR (400 MHz, DMSO, 25 °C, TMS) δ = 8.26 (s, 1H), 8.26−8.17 (m, 2H), 8.07 (s, 1H), 7.53−7.49 (m, 8H), 7.38−7.34 (m, 7H), 7.24−7.19 (m, 2H), 3.53 ppm (s, 3H); ^{13}C NMR (100 MHz, DMSO, 25 °C, TMS) δ = 195.4, 165.2, 147.2, 142.4, 139.5, 137.8, 137.5, 137.2, 137.0, 134.9, 133.1, 133.0, 132.2, 130.7, 129.5, 128.5, 128.4, 128.4, 128.3, 128.2, 128.0, 123.0, 52.7; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{39}H_{26}NO_8$ 636.1653, found 636.1647.

*6-(Ethoxycarbonyl)-7-(4-methoxybenzoyl)-3-(4-methylbenzoyl)-4-pentyl-8-phenyl-2-naphthoic Acid (**5lj**).* A mixture of **1l** (57.3 mg, 0.2 mmol), ester **2j** (194.6 mg, 0.6 mmol), $PdCl_2$ (1.8 mg, 0.01 mmol), and CuI (38.1 mg, 0.2 mmol) in DMF (2.0 mL) was stirred at 60 °C under O_2 for 1 h. The crude product was purified by column chromatography on silica gel (n-hexane/acetone = 3:1, v/v) to afford **5lj** (97.7 mg, 76%) and **2j** (129.7 mg, 0.40 mmol): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.83 (s, 1H), 8.15 (s, 1H), 7.55 (d, J = 7.2 Hz, 2H), 7.48 (d, J = 8.4 Hz, 2H), 7.19−7.09 (m, 7H), 6.69 (d, J = 8.8 Hz, 2H), 4.16−4.10 (m, 2H), 3.73 (s, 3H), 3.06−2.67 (m, 2H), 2.30 (s, 3H), 1.71−1.42 (m, 2H), 1.33−1.16 (m, 4H), 1.05 (t, J = 7.2 Hz, 3H), 0.77 ppm (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 195.4, 165.7, 163.1, 140.5, 138.8, 137.9, 135.5, 135.5, 133.2, 131.3, 131.3, 129.3, 129.0, 129.0, 128.7, 128.1, 128.0, 128.0, 127.9, 127.9, 127.7, 61.9, 55.4, 32.1, 31.1, 30.1, 22.1, 21.7, 13.9, 13.7; HRMS (ESI) m/z $[M + H]^+$ calcd for$C_{41}H_{39}O_7$ 643.2690, found 643.2698.

*2,6-Dibenzoyl-3-(methoxycarbonyl)-5-phenyl-[1,1′-binaphthalene]-7-carboxylic Acid (**5id**).* A mixture of acid **1i** (64.5 mg, 0.2 mmol), ester **2d** (171.8 mg, 0.6 mmol), $PdCl_2$ (1.8 mg, 0.01 mmol), and CuI (38.1 mg, 0.2 mmol) in DMF (2.0 mL) was stirred at 60 °C under O_2 for 1 h. The crude product was purified by column

DOI: 10.1021/acs.joc.5b02870
J. Org. Chem. 2016, 81, 2770−2781

chromatography on silica gel (*n*-hexane/acetone = 3:1, v/v) to afford **5id** (98.7 mg, 77%) and **2b** (106.0 mg, 0.36 mmol): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.31 (d, J = 0.4 Hz, 1H), 7.94 (s, 1H), 7.68 (d, J = 8.0 Hz, 2H), 7.31−7.28 (m, 6H), 7.25−7.21 (m, 5H), 7.17−6.97 (m, 9H), 3.51 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 195.5, 168.0, 165.1, 138.8, 138.5, 137.4, 136.7, 136.2, 133.9, 133.0, 132.8, 132.0, 131.4, 131.3, 131.2, 129.9, 129.7, 129.0, 128.5, 128.4, 128.2, 127.7, 127.5, 127.2, 127.2, 127.0, 126.9, 126.7, 125.3, 125.0, 123.7, 51.5; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{43}H_{29}O_6$ 641.1959, found 641.1961.

Synthesis of Compound 6ab. Diphenylphosphoryl azide (165.1 mg, 0.6 mmol) and triethylamine (60.6 mg, 0.6 mmol) were added to a solution of **5ab** (119.6 mg, 0.2 mmol) in 1,4-dioxane (3.0 mL) at 25 °C. The mixture was stirred for 12 h and then evaporated under reduced pressure. After the addition of TFA (3 mL), the resulting mixture was stirred at 80 °C for 2 h and then cooled to 0 °C, neutralized with saturated aqueous Na_2CO_3 solution, and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated in vacuum, and the residue was purified by flash column chromatography on silica gel (*n*-hexane/EtOAc = 5:1, v/v) to afford product **6ab** (70.6 mg, 62%).

*Ethyl 6-amino-3,7-dibenzoyl-8-pentyl-4-phenyl-2-naphthoate (**6ab**):* ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.73 (m, 1H), 7.83 (d, J = 7.2 Hz, 2H), 7.58−7.52 (m, 3H), 7.43−7.39 (m, 2H), 7.35−7.31 (m, 1H), 7.22−7.13 (m, 7H), 6.47 (s, 1H), 4.12−4.06 (m, 2H), 3.78 (s, 2H), 2.84−2.80 (m, 2H), 1.59−1.55 (m, 2H), 1.24−1.18 (m, 4H), 1.01 (t, J = 7.2 Hz, 3H), 0.77 ppm (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 199.3, 197.5, 166.3, 143.7, 139.7, 138.4, 137.7, 137.1, 137.0, 136.7, 136.4, 134.4, 132.4, 129.6, 129.0, 128.9, 128.8, 128.4, 128.0, 127.8, 127.5, 125.0, 122.6, 107.4, 61.3, 32.0, 31.3, 30.7, 22.2, 13.9, 13.7; HRMS (EI) m/z [M]$^+$ calcd for $C_{38}H_{35}NO_4$ 569.2566, found 569.2561.

Synthesis of Compound 7ab. An oven-dried vessel was charged with **5ab** (119.6 mg, 0.2 mmol), Cu_2O (11.4 mg, 0.08 mmol), and 1,10-phenanthroline (14.4 mg, 0.08 mmol). After the vessel was purged with alternating vacuum and nitrogen cycles, a degassed solution of NMP (0.9 mL) and quinoline (0.3 mL) was added via syringe. The resulting mixture was stirred for 12 h at 170 °C, acidized by aqueous 3 N HCl, and extracted repeatedly with diethyl ether. The combined organic layers were washed with brine, dried over Na_2SO_4, and filtered, the solvent was removed under vacuum, and the residue was purified through column chromatography (silica gel, eluent: petroleum ether/acetone = 10:1) to afford the pure product **7ab** (103.2 mg, 93%).

*Ethyl 3,7-dibenzoyl-8-pentyl-4-phenyl-2-naphthoate (**7ab**):* ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.95 (s, 1H), 7.76−7.73 (m, 2H), 7.54−7.51 (m, 3H), 7.40−7.33 (m, 4H), 7.32−7.26 (m, 1H), 7.22−7.18 (m, 2H), 7.14 (s, 3H), 7.06 (s, 2H), 4.16−4.11 (m, 2H), 3.09−3.05 (m, 2H), 1.72−1.68 (m, 2H), 1.35−1.26 (m, 4H), 1.04 (t, J = 6.8 Hz, 3H), 0.80 ppm (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 198.1, 196.7, 165.6, 139.0, 138.6, 138.0, 137.0, 136.8, 135.6, 134.8, 133.2, 132.1, 130.7, 130.4, 129.7, 128.5, 128.1, 127.9, 127.6, 127.3, 127.3, 126.8, 126.2, 124.2, 61.3, 31.6, 31.3, 29.5, 21.8, 13.5, 13.2; HRMS (EI) m/z [M]$^+$ calcd for $C_{38}H_{34}O_4$ 554.2457, found 554.2459.

Synthesis of Compound 8ab. A dry 10 mL round flask was charged with a solution of **1a** (54.5 mg, 0.2 mmol), **2b** (194.6 mg, 0.6 mmol), $PdCl_2$ (35.5 mg, 0.2 mmol), CuI (38.1 mg, 0.2 mmol), and TEMPO (62.5 mg, 0.4 mmol) in DMF (2.0 mL) under N_2 atmosphere at 60 °C for 1 h. The solvent was concentrated under vacuum, and the residue was purified through a short column chromatography to afford the pure product **8ab** (91.5 mg, 67%).

*Ethyl 7-benzoyl-1-oxo-4-pentyl-3,8-diphenyl-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)-1,3-dihydronaphtho[2,3-c]furan-6-carboxylate (**8ab**):* ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS) δ = 8.86 (s, 1H), 8.64 (s, 1H), 7.59−7.56 (m, 4H), 7.43−7.34 (m, 2H), 7.28−7.06 (m, 9H), 4.23−4.15 (m, 2H), 3.23−3.07 (m, 2H), 1.61−1.52 (m, 3H), 1.42 (s, 3H), 1.39−1.24 (m, 6H), 1.21 (s, 6H), 1.17−1.12 (m, 2H), 1.08 (t, J = 7.2 Hz, 3H), 0.84 (t, J = 7.2 Hz, 3H), 0.18−0.13 (m, 1H), 0.00 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ = 196.9, 168.9, 165.7, 144.5, 141.0, 139.9, 137.9, 137.7, 137.6, 135.8, 135.4, 134.6, 132.8, 131.0, 130.6, 129.0, 128.8, 128.4, 128.4, 128.2, 128.1, 128.0, 127.9, 126.8, 126.5, 123.3, 107.5, 61.9, 61.9, 59.8, 40.9, 40.6, 34.8, 33.9, 32.5, 29.2, 28.5, 22.3, 22.0, 21.4, 17.0, 14.1, 13.6; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{48}H_{52}NO_6$ 738.3789, found 738.3778.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02870.

Experimental procedures and spectral data for all new compounds (PDF)

X-ray crystallographic data of **4h′** (CIF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: mcorg@zju.edu.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the National Natural Science Foundation of China (21372196 and 21572199) for generous financial support.

■ REFERENCES

(1) For reviews, see: (a) de Koning, C. B.; Rousseau, A. L.; van Otterlo, W. A. L. *Tetrahedron* **2003**, *59*, 7. (b) Jin, T.; Zhao, J.; Asao, N.; Yamamoto, Y. *Chem. - Eur. J.* **2014**, *20*, 3554.

(2) (a) Jones, R. R.; Bergman, R. G. *J. Am. Chem. Soc.* **1972**, *94*, 660. (b) Bergman, R. G. *Acc. Chem. Res.* **1973**, *6*, 25.

(3) For recent reviews, see: (a) Chinchilla, R.; Nájera, C. *Chem. Rev.* **2014**, *114*, 1783. (b) Luo, Y.; Pan, X.; Yu, X.; Wu, J. *Chem. Soc. Rev.* **2014**, *43*, 834. (c) Ohno, H. *Asian J. Org. Chem.* **2013**, *2*, 18. (d) Vlaar, T.; Ruijter, E.; Orru, R. V. A. *Adv. Synth. Catal.* **2011**, *353*, 809. (e) Deng, Y.-Q.; Persson, A. K. Å; Bäckvall, J.-E. *Chem. - Eur. J.* **2012**, *18*, 11498. (f) Alabugin, I. V.; Gold, B. *J. Org. Chem.* **2013**, *78*, 7777.

(4) (a) Alabugin, I. V.; Gilmore, K.; Patil, S.; Manoharan, M.; Kovalenko, S. V.; Clark, R. J.; Ghiviriga, I. *J. Am. Chem. Soc.* **2008**, *130*, 11535. (b) Byers, P. M.; Alabugin, I. V. *J. Am. Chem. Soc.* **2012**, *134*, 9609. (c) Pati, K.; dos Passos Gomes, G.; Harris, T.; Hughes, A.; Phan, H.; Banerjee, T.; Hanson, K.; Alabugin, I. V. *J. Am. Chem. Soc.* **2015**, *137*, 1165.

(5) For reviews, see: (a) Mohamed, R. K.; Peterson, P. W.; Alabugin, I. V. *Chem. Rev.* **2013**, *113*, 7089. (b) Hashmi, A. S. K. *Acc. Chem. Res.* **2014**, *47*, 864. For leading references, see: (c) Wang, Y.; Finn, M. G. *J. Am. Chem. Soc.* **1995**, *117*, 8045. (d) Ohe, K.; Kojima, M.; Yonehara, K.; Uemura, S. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1823.

(6) For selected references, see: (a) O'Connor, J. M.; Friese, S. J.; Rodgers, B. L. *J. Am. Chem. Soc.* **2005**, *127*, 16342. (b) Odedra, A.; Wu, C.-J.; Pratap, T. B.; Huang, C.-W.; Ran, Y.-F.; Liu, R.-S. *J. Am. Chem. Soc.* **2005**, *127*, 3406. (c) Lee, C.-Y.; Wu, M.-J. *Eur. J. Org. Chem.* **2007**, *2007*, 3463. (d) Hirano, K.; Inaba, Y.; Watanabe, T.; Oishi, S.; Fujii, N.; Ohno, H. *Adv. Synth. Catal.* **2010**, *352*, 368. (e) Ye, L.; Wang, Y.; Aue, D. H.; Zhang, L. *J. Am. Chem. Soc.* **2012**, *134*, 31. (f) Hashmi, A. S. K.; Braun, I.; Rudolph, M.; Rominger, F. *Organometallics* **2012**, *31*, 644. (g) Byers, P. M.; Rashid, J. I.; Mohamed, R. K.; Alabugin, I. V. *Org. Lett.* **2012**, *14*, 6032. (h) Hou, Q.; Zhang, Z.; Kong, F.; Wang, S.; Wang, H.; Yao, Z.-J. *Chem. Commun.* **2013**, *49*, 695. (i) Campolo, D.; Arif, T.; Borie, C.; Mouysset, D.; Vanthuyne, N.; Naubron, J.-V.; Bertrand, M. P.; Nechab, M. *Angew. Chem., Int. Ed.* **2014**, *53*, 3227.

(7) (a) Saxena, A.; Perez, F.; Krische, M. J. *J. Am. Chem. Soc.* **2015**, *137*, 5883. (b) Ling, F.; Li, Z.; Zheng, C.; Liu, X.; Ma, C. *J. Am. Chem. Soc.* **2014**, *136*, 10914.

DOI: 10.1021/acs.joc.5b02870
J. Org. Chem. 2016, 81, 2770−2781

(8) Trost, B. M. *Science* **1983**, *219*, 245.
(9) For our related studies, see: (a) Wang, D.; Ling, F.; Liu, X.; Li, Z.; Ma, C. *Chem. - Eur. J.* **2016**, *22*, 124. (b) Li, Z.; Ling, F.; Cheng, D.; Ma, C. *Org. Lett.* **2014**, *16*, 1822. (c) Cheng, D.; Ling, F.; Li, Z.; Yao, W.; Ma, C. *Org. Lett.* **2012**, *14*, 3146. (d) Yao, W.; Pan, L.; Zhang, Y.; Wang, G.; Wang, X.; Ma, C. *Angew. Chem., Int. Ed.* **2010**, *49*, 9210.
(10) For a recent review on the synthesis of aryl ketones via C−H activation, see: Wu, X.-F. *Chem. - Eur. J.* **2015**, *21*, 12252.
(11) For recent reviews on palladium-catalyzed cascade reactions, see: (a) Chinchilla, R.; Nájera, C. *Chem. Rev.* **2014**, *114*, 1783. (b) Luo, Y.; Pan, X.; Yu, X.; Wu, J. *Chem. Soc. Rev.* **2014**, *43*, 834. (c) Ohno, H. *Asian J. Org. Chem.* **2013**, *2*, 18. (d) Deng, Y.-Q.; Persson, A. K. Å.; Bäckvall, J.-E. *Chem. - Eur. J.* **2012**, *18*, 11498. (e) Vlaar, T.; Ruijter, E.; Orru, R. V. A. *Adv. Synth. Catal.* **2011**, *353*, 809.
(12) For a review on Pd-catalyzed oxidation of alkynes, see: (a) Muzart, J. *J. Mol. Catal. A: Chem.* **2011**, *338*, 7. For reviews on Pd-catalyzed aerobic transformations, see: (b) Wu, W.; Jiang, H. *Acc. Chem. Res.* **2012**, *45*, 1736. (c) Shi, Z.; Zhang, C.; Tang, C.; Jiao, N. *Chem. Soc. Rev.* **2012**, *41*, 3381. (d) Gligorich, K. M.; Sigman, M. S. *Chem. Commun.* **2009**, 3854. (e) Stahl, S. S. *Angew. Chem., Int. Ed.* **2004**, *43*, 3400.
(13) For selected reviews, see: (a) Lörtscher, E. *ChemPhysChem* **2011**, *12*, 2887. (b) Lambert, C. *Angew. Chem., Int. Ed.* **2011**, *50*, 1756. (c) Suraru, S.-L.; Würthner, F. *Angew. Chem., Int. Ed.* **2014**, *53*, 7428. (d) Chakrabarty, R.; Mukherjee, P. S.; Stang, P. J. *Chem. Rev.* **2011**, *111*, 6810.
(14) For a review on the synthesis of enediyne, see: Rossi, R.; Bellina, F.; Lessi, M.; Manzini, C. *Tetrahedron* **2013**, *69*, 7869.
(15) For a general review on aerobic copper-catalyzed reactions, see: Allen, S. E.; Walvoord, R. R.; Padilla-Salinas, R.; Kozlowski, M. C. *Chem. Rev.* **2013**, *113*, 6234.
(16) For Cu-catalyzed oxidative amidation−diketonization of terminal alkynes using dioxygen, see: (a) Zhang, C.; Jiao, N. *J. Am. Chem. Soc.* **2010**, *132*, 28. For the Pd-catalyzed cleavage reaction of alkynes with dioxygen, see: (b) Wang, A.; Jiang, H. *J. Am. Chem. Soc.* **2008**, *130*, 5030.
(17) For a discussion on the Baldwin's ring closure rules, see: Alabugin, I. V.; Gilmore, K. *Chem. Commun.* **2013**, *49*, 11246.
(18) For a recent review of Wacker oxidation, see: (a) Sigman, M. S.; Werner, E. W. *Acc. Chem. Res.* **2012**, *45*, 874. For Pd-catalyzed diketonization of alkynes with H_2O, see: (b) Ren, W.; Xia, Y.; Ji, S.-J.; Zhang, Y.; Wan, X.; Zhao, J. *Org. Lett.* **2009**, *11*, 1841.
(19) For a recent review of Cu-catalyzed transformation via a single-electron-transfer process, see: (a) Zhang, C.; Tang, C.; Jiao, N. *Chem. Soc. Rev.* **2012**, *41*, 3464. For one-electron oxidation of 1,3-dien-2-ol, see: (b) Schmittel, M.; Langels, A. *Liebigs Ann.* **1996**, *1996*, 999.
(20) For selected examples, see: (a) Lu, Q.; Zhang, J.; Wei, F.; Qi, Y.; Wang, H.; Liu, Z.; Lei, A. *Angew. Chem., Int. Ed.* **2013**, *52*, 7156. (b) Wang, Y.-F.; Chen, H.; Zhu, X.; Chiba, S. *J. Am. Chem. Soc.* **2012**, *134*, 11980. For a report on the Fenton mechanism, see: (c) Rachmilovich-Calis, S.; Masarwa, A.; Meyerstein, N.; Meyerstein, D.; van Eldik, R. *Chem. - Eur. J.* **2009**, *15*, 8303.
(21) For selected reviews, see: (a) Bielski, R.; Witczak, Z. *Chem. Rev.* **2013**, *113*, 2205. (b) Rousseau, G.; Breit, B. *Angew. Chem., Int. Ed.* **2011**, *50*, 2450.

DOI: 10.1021/acs.joc.5b02870
J. Org. Chem. 2016, 81, 2770−2781