JOC The Journal of Organic Chemistry

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Naphthoquinone-Directed C−H Annulation and C_{sp^3}−H Bond Cleavage: One-Pot Synthesis of Tetracyclic Naphthoxazoles

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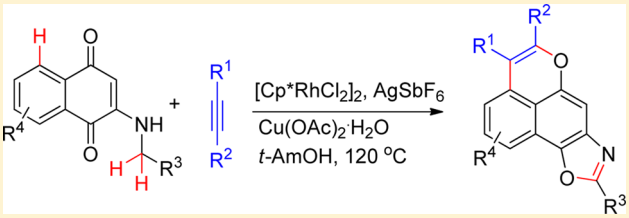
Supporting Information

ABSTRACT: One-pot synthesis of tetracyclic naphthoxazole derivatives from electron-deficient naphthoquinones and alkynes was achieved via Rh(III)-catalyzed C−H activation and C_{sp^3}−H bond cleavage for the first time. This approach proceeds through a tandem cascade process involving substrate tautomerization, C−H activation, oxidative addition, cyclization, and aromatization. In addition, broad substrate scope, simple starting materials, and steric tolerance make this strategy of great practicality.



INTRODUCTION

Naphthoxazoles fused with an additional aryl or aliphatic ring are present in many biologically active and pharmaceutically relevant natural products and synthetic analogues and, therefore, constitute challenging molecular targets for both synthetic and medicinal chemistry studies.[1] For example, pseudopteroxazole **1** (Figure 1) is a marine natural product

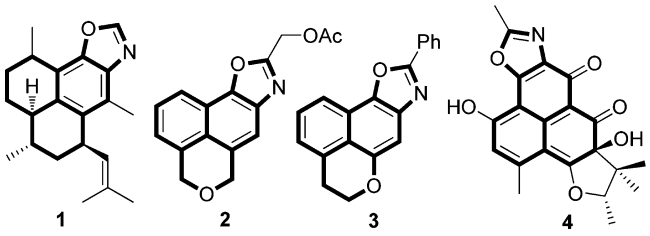


Figure 1. Biologically active tetracyclic naphthoxazoles.

isolated in 1999 possessing potent growth inhibition against *Mycobacterium tuberculosis* H37Rv.[1a] Compounds **2** and **3** are cytotoxic agents capable of intercalating into the DNA base pairs.[1d,e] Herqueioxazole **4** was isolated very recently as a metabolite of marine-derived fungus *Penicillium sp.* showing significant inhibition against *Staphylococcus aureus* sortase A.[1f] Despite that numerous preparative methods for bicyclic benzoxazoles and tricyclic naphthoxazoles are available,[2] synthetic strategies toward complex frameworks of tetracyclic naphthoxazoles using simple starting materials through a one-pot process have not been reported yet.

Rh(III)-catalyzed oxidative coupling of arenes with alkynes has been extensively explored recently.[3−5] This approach not only allows convenient synthesis of various bi- or tricyclic compounds but also enables the construction of structurally more complex tetraheterocycles as the 1:2 coupling products.[4p] With the hydroxyl group of 1-naphthol as the directing group, Miura's group reported a highly efficient synthesis of naphthopyrans through a Rh-catalyzed oxidative annulation (eq 1, Scheme 1).[4c] Since the tautomerization of quinones to the corresponding phenols is common, we envisioned that quinones themselves might be used directly as "masked" phenolic substrates to trigger similar C−H activations. To the best of our knowledge, direct usage of the electron-deficient quinones as the directing group in Rh-catalyzed C−H functionalization has not been reported yet.[5] Herein, we present the first example of naphthoquinone-induced Rh(III)-catalyzed C−H activation combined with a C_{sp^3}−H bond cleavage, leading to the tetracyclic naphthoxazole networks formed in a one-pot reaction (eq 2, Scheme 1). The structural novelty of reaction products and high efficiency of such a one-pot process, together with the wide substrate scope, make this approach highly appealing.

RESULTS AND DISCUSSION

Our initial experiment was performed by treating 2-propylamino-1,4-naphthoquinone (**5a**) with diphenylacetylene (**6a**, 1.5 equiv) in the presence of $[Cp^*RhCl_2]_2$ (0.05 equiv) and $Cu(OAc)_2·H_2O$ (2 equiv) in *t*-AmOH at 100 °C for 6 h. To our delight, tetracyclic naphthoxazole **7aa** was obtained in 12% yield, along with a small amount of naphthoxazole acetate **8aa** (Table 1, entry 1). To improve the yield of **7aa**, we conducted a systematic optimization of the reaction conditions. It was found that $AgSbF_6$ is a critical enhancer to the yield (entry 4). The side product could be greatly suppressed by lowering the $Cu(OAc)_2·H_2O$ loading; however, the yield of **7aa**

Received: March 11, 2014
Published: April 18, 2014

   dx.doi.org/10.1021/jo500572u | J. Org. Chem. 2014, 79, 4553−4560

Scheme 1. Rh(III)-Catalyzed Phenol-Directed Oxidative Coupling and Our Work

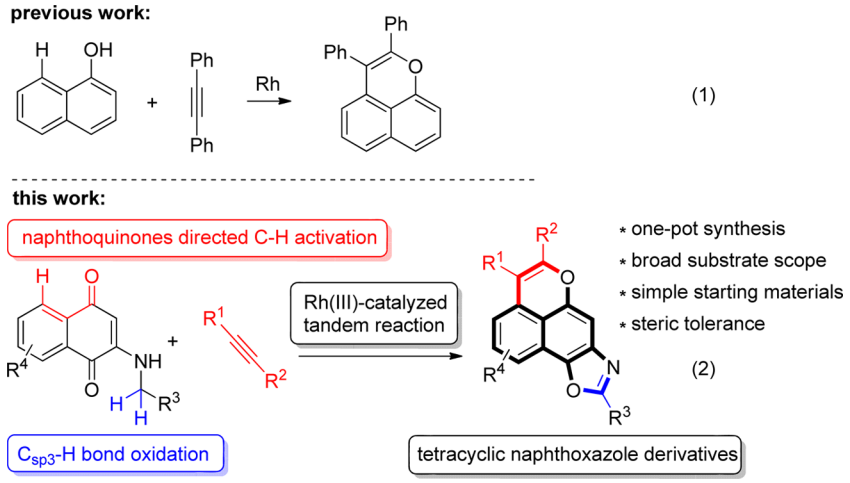
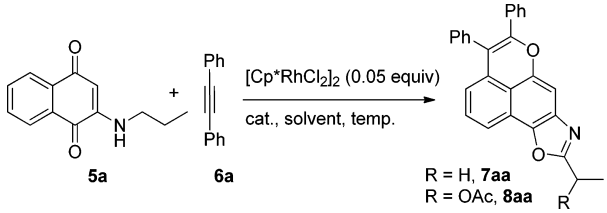


Table 1. Optimization of the Reaction Conditions[a,b]



entry	catalytic system (amount [equiv])	solvent	T (°C)	7aa:8aa	yield of 7aa (%)
1	$Cu(OAc)_2·H_2O$ (2)	*t*-AmOH	100	6:1	12
2	$Cu(OAc)_2·H_2O$ (2)[c]	*t*-AmOH	120		
3	$AgSbF_6$ (0.2)	*t*-AmOH	120		
4	$Cu(OAc)_2·H_2O$ (2)/$AgSbF_6$ (0.2)	*t*-AmOH	100	5:1	53
5	**$Cu(OAc)_2·H_2O$ (2)/$AgSbF_6$ (0.2)**	***t*-AmOH**	**120**	**6:1**	**73**
6	$Cu(OAc)_2·H_2O$ (2)/$AgSbF_6$ (0.2)/AgOAc (2)	*t*-AmOH	120	4:1	66
7	$Cu(OAc)_2·H_2O$ (0.5)/Ag_2CO_3 (1)	*t*-AmOH	120	3:1	33
8	$Cu(OAc)_2·H_2O$ (0.5)/$AgSbF_6$ (0.2)/$Mn(OAc)_3·2H_2O$ (1.5)	*t*-AmOH	120	14:1	59
9	$AgSbF_6$ (0.2)/$Mn(OAc)_3·2H_2O$ (2)	*t*-AmOH	120	9:1	26
10	$Cu(OAc)_2·H_2O$ (1)/$AgSbF_6$ (0.2)	*t*-AmOH	120	19:1	39
11	$Cu(OAc)_2·H_2O$ (2)/$AgSbF_6$ (0.2)	HFIP	70	5:1	37
12	$[Ru(p\text{-cymene})Cl_2]_2$ (0.05)/$Cu(OAc)_2·H_2O$ (2)[c]	*m*-xylene	100	100-	<5
13	$[Cp^*IrCl_2]_2$ (0.05)/$Cu(OAc)_2·H_2O$ (2)[c]	*t*-AmOH	120	100-	<5
14	$Cu(OAc)_2·H_2O$ (1.5)/$AgSbF_6$ (0.2)/O_2	*t*-AmOH	120	19:1	62
15	$Cu(OAc)_2·H_2O$ (2)/$AgSbF_6$ (0.2)/TEMPO (2)	*t*-AmOH	120	6:1	68
16	$Cu(OAc)_2·H_2O$ (2)/$AgSbF_6$ (0.1)/H_2O (5)	*t*-AmOH	120	4.6:1	64

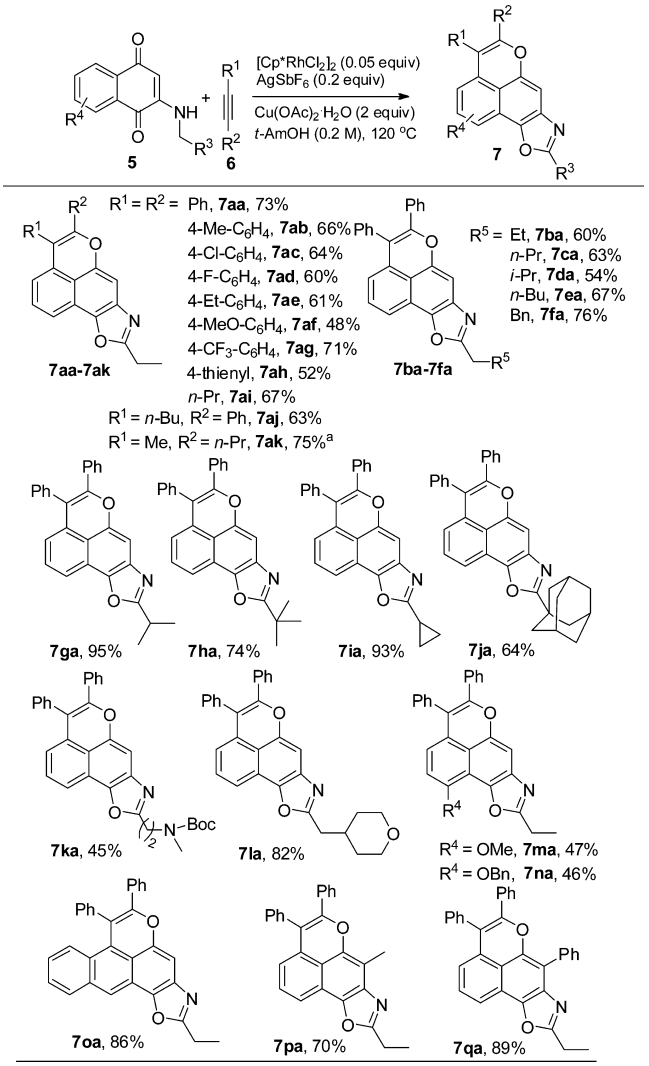
[a]Conditions: A mixture of naphthoquinone (0.1 mmol), alkyne (0.15 mmol), catalyst, and solvent (0.5 mL) was stirred in sealed tubes at 120 °C for 6 h. [b]Isolated yields. [c]Without $[Cp^*RhCl_2]_2$

was also reduced (entry 10). Cooxidants were also used, but the total yields were low (entries 6−8 and 14). Control experiments showed that no product was observed in the absence of either $[Cp^*RhCl_2]_2$ (entry 2) or $Cu(OAc)_2·H_2O$ (entry 3). Water had little influence on the reaction yield (entry 16). Finally, a high yield of 73% was achieved for **7aa** by using $[Cp^*RhCl_2]_2$ (0.05 equiv), $Cu(OAc)_2·H_2O$ (2 equiv), and $AgSbF_6$ (0.2 equiv) in *t*-AmOH at 120 °C for 6 h (entry 5).

Next, we set out to investigate the scope of this transformation (Scheme 2). First, with 2-propylamino-1,4-naphthoquinone (**5a**) as the model substrate, a series of alkynes **6** were tested as the coupling partners. All the reactions proceeded smoothly, and products **7ab**−**7ak** were obtained in moderate to good yields. Reactions using terminal alkynes and TMS-protected alkynes failed. It was found that substrates **5** bearing various *N*-alkyl substituents reacted with diphenylacetylene **6a** smoothly, and the corresponding naphthoxazoles **7ba**−**7fa** were obtained in 54−76% yields. Surprisingly, naphthoquinones **5** containing a bulky *N*-alkyl group were well-tolerated, and products **7ga** and **7ia** were obtained in high yields of 95% and 93%. Substrates **5** with a larger *N*-substituent gave corresponding products **7ha** and **7ja** in 74% and 64% yields, respectively. Notably, functionalized *N*-alkyl in 1,4-naphthoquinone **5** was stable, and compound **7ka** was obtained in 45% yield. Much higher yield (82%) was achieved for the morpholine-substituted product **7la**. Finally, variations in the 1,4-naphthoquinone skeleton of **5** were exploited as well (Scheme 2). Introducing a MeO− or BnO− to the phenyl ring was acceptable, although the yields were somewhat lower (47% for **7ma**, 46% for **7na**). However, fusing an additional phenyl

dx.doi.org/10.1021/jo500572u | J. Org. Chem. 2014, 79, 4553−4560

Scheme 2. Substrate Scope of the Tandem Reaction[a,b]



[a]Regioisomeric ratios were determined as 1:1 by respective isolated yields.

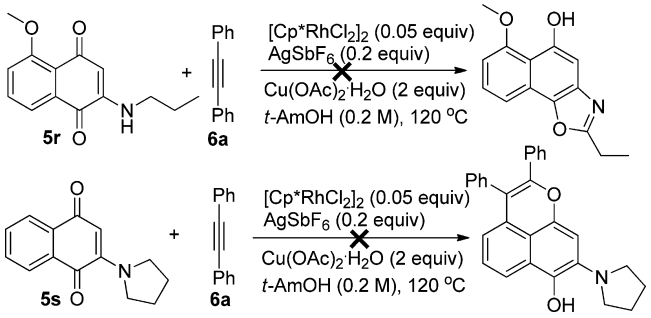
[b]Reaction conditions: **5a**–**5q** (0.4 mmol), **6a**–**6k** (0.6 mmol), $[Cp^*RhCl_2]_2$ (0.05 equiv), $Cu(OAc)_2{\cdot}H_2O$ (2 equiv), $AgSbF_6$ (0.2 equiv), *t*-AmOH (2 mL), sealed tubes, 120 °C, 6 h.

ring to the naphthoquinone system led to formation of pentacyclic product **7oa** in high yield (86%). Substrates **5p** and **5q** with a methyl or phenyl group on the benzoquinonyl ring also went through the reaction smoothly, and products **7pa** and **7qa** were obtained in 70% and 89% yields, respectively.

All the compounds were fully characterized by spectroscopic data, and their structures were further confirmed by the single-crystal X-ray analysis of **7aa** (see the Supporting Information). To validate the efficiency and practicality of this cascade reaction, coupling of 2-propylamino-1,4-naphthoquinone (**5a**) and diphenylacetylene (**6a**) was conducted on a gram scale, and tetracyclic product **7aa** was delivered smoothly without significant loss of the yield.

To gain some mechanistic insights to the present cascade process, several supplementary reactions were performed. As shown in Scheme 3, we first tested the reactions of alkyne **6a** with 5-methoxy-2-(propylamino)-1,4-naphthoquinone (**5r**) and 2-(pyrrolidin-1-yl)-1,4-naphthoquinone (**5s**) and found that no

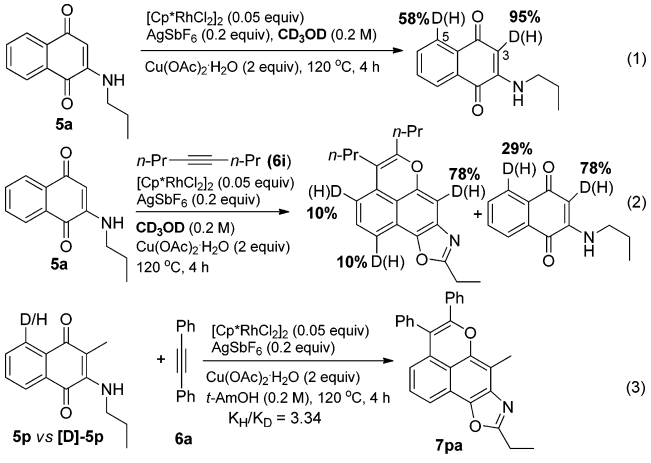
Scheme 3. Reaction of 6a with Naphthoquinolines 5r and 5s



products formed. Besides, simple naphthoquinone lacking the amino substituent did not give the corresponding product under the same conditions, either. These results suggested that the reaction likely proceeded in a tandem cascade fashion rather than stepwise, and both the aromatic H-5 and free N-H are necessary to initiate the catalytic reaction. In addition, to determine whether a Cu(II)-catalyzed radical process[6] was involved in the reaction, TEMPO was added as a radical scavenger to the reaction of **5a** and **6a**, and no significant loss in the yield of **7aa** was observed (Table 1, entry 15).

Further, a series of deuterium-labeling experiments were conducted. It was found that, in the absence of acetylene **6a**, treating substrate **5a** along with $[Cp^*RhCl_2]_2$, $AgSbF_6$, and $Cu(OAc)_2{\cdot}H_2O$ in CD_3OD resulted in the partially deuterated reactant at 3- and 5-positions (eq 1, Scheme 4), indicating that

Scheme 4. Experiments with Isotopically Labeled Compounds

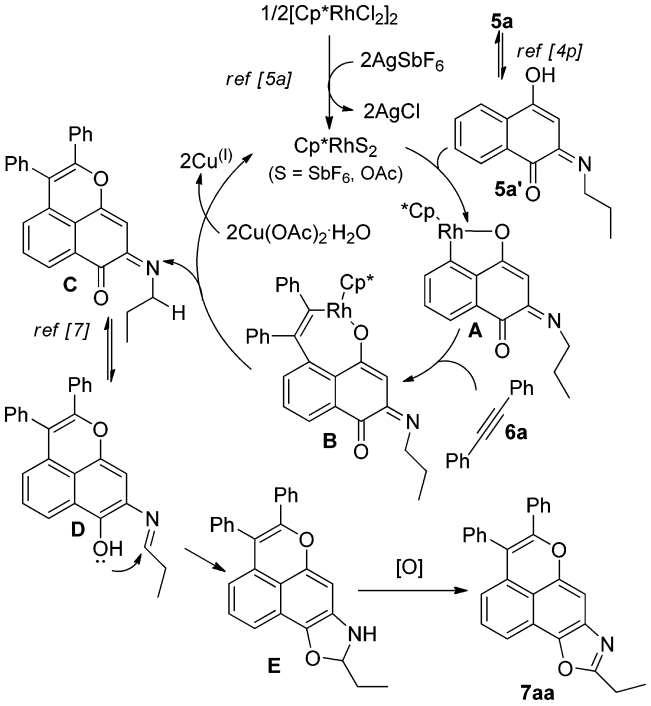


the C–H activation is reversible. Further, it was found that reaction of **5a** and **6i** in the presence of CD_3OD led to both deuterated product and recovered reactant (eq 2), suggesting that the cascade reaction was ignited by the C_5–H activation. In addition, two parallel independent reactions of substrates **5p** and [D-5]-**5p** with **6a** demonstrated a kinetic isotope effect (KIE) of $K_H/K_D = 3.34$. These results indicated that cleavage of the C_5–H bond was involved in the rate-determining step.

On the basis of the results above, a plausible mechanism was proposed to the present catalytic process. As shown in Scheme 5, the reaction cycle is likely started by tautomerization of **5a** to phenol **5a′**, which then undergoes a well-known Rh(III)-catalyzed C–H activation to form a five-membered rhodacycle **A**.[3,4] Insertion of alkyne **6a** to the Rh–C_{phenyl} bond would

dx.doi.org/10.1021/jo500572u | J. Org. Chem. 2014, 79, 4553–4560

Scheme 5. Proposed Mechanistic Pathway



produce a seven-membered species **B**. Subsequent reductive elimination of the intermediate **B** leads to formation of intermediate **C**. Rh(III) would be regenerated under the oxidation of $Cu(OAc)_2·H_2O$. The intermediate **C** would then proceed through a C_{sp^3}–H cleavage/shift[7] to form intermediate **D**, which then undergoes a cyclization, followed by oxidative aromatization, to yield final product **7aa**.

In summary, we have developed a rhodium-catalyzed process to construct tetracyclic naphthoxazole derivatives by oxidative coupling of electron-deficient quinones with alkynes. Mechanism studies indicated that this one-pot reaction involves a tandem cascade process including tautomerization/C–H activation/oxidative addition/cyclization/aromatization. This protocol not only represents a novel one-pot approach to access the tetracyclic naphthoxazoles but also showcases the capacity of combining a C–H activation and a C_{sp^3}–H bond cleavage to form a heterocyclic complex for the first time.

EXPERIMENTAL SECTION

General Information. All reactions were performed in glassware containing a Teflon-coated stir bar. All solvents and chemical reagents were obtained from commercial sources and used without further purifications. ^1H and ^{13}C NMR spectra were recorded with tetramethylsilane as an internal reference. High-resolution mass spectrometry (HRMS) analysis was recorded by electrospray ionization (ESI-TOF). Flash column chromatography on silica gel (200–300 mesh) was used for the routine purification of reaction products. The column output was monitored by TLC on silica gel (100–200 mesh) precoated on glass plates (15 × 50 mm), and spots were visualized by UV light at 254 or 365 nm. Alkynes **6** were purchased or prepared according to the literature.[8] Substrates **5** were either commercially available or prepared by following literature procedures.[9]

General Procedure for Preparation of 2-Amino-1,4-naphthoquinones 5. To a solution of naphthoquinones (5 mmol) in MeOH (10 mL) were added amines (5 mmol) slowly. The mixture was stirred at room temperature for 1 h, concentrated in vacuo, and then purified by column chromatography to give the 2-amino-1,4-naphthoquinones **5**.

*2-(Propylamino)naphthalene-1,4-dione (**5a**).* Red solid. ^1H NMR (300 MHz, $CDCl_3$): δ 8.09 (d, J = 7.6 Hz, 1H), 8.04 (d, J = 7.7 Hz, 1H), 7.72 (t, J = 7.6 Hz, 1H), 7.60 (t, J = 7.5 Hz, 1H), 5.90 (brs, 1H), 5.73 (s, 1H), 3.15 (m, 2H), 1.72 (m, 2H), 1.02 (t, J = 7.4 Hz, 3H).

*2-(Butylamino)naphthalene-1,4-dione (**5b**).* Red solid. ^1H NMR (300 MHz, $CDCl_3$): δ 8.07 (d, J = 7.6 Hz, 1H), 8.01 (d, J = 7.6 Hz, 1H), 7.69 (m, 1H), 7.58 (m, 1H), 5.87 (brs, 1H), 5.70 (s, 1H), 3.15 (m, 2H), 1.65 (m, 2H), 1.41 (m, 2H), 0.94 (t, J = 7.3 Hz, 3H).

*2-(Pentylamino)naphthalene-1,4-dione (**5c**).* Red solid. ^1H NMR (300 MHz, $CDCl_3$): δ 8.07 (d, J = 7.6 Hz, 1H), 8.01 (d, J = 7.6 Hz, 1H), 7.70 (t, J = 7.5 Hz, 1H), 7.58 (t, J = 7.5 Hz, 1H), 5.88 (brs, 1H), 5.70 (s, 1H), 3.15 (m, 2H), 1.67 (m, 2H), 1.36 (m, 4H), 0.90 (t, J = 6.6 Hz, 3H).

*2-(Isopentylamino)naphthalene-1,4-dione (**5d**).* Red solid. ^1H NMR (300 MHz, $CDCl_3$): δ 8.08 (d, J = 7.6 Hz, 1H), 8.01 (d, J = 7.6 Hz, 1H), 7.70 (td, J = 7.5, 1.2 Hz, 1H), 7.58 (td, J = 7.5, 1.2 Hz, 1H), 5.84 (brs, 1H), 5.71 (s, 1H), 3.17 (m, 2H), 1.67 (m, 1H), 1.56 (m, 2H), 0.94 (d, J = 6.5 Hz, 6H).

*2-(Hexylamino)naphthalene-1,4-dione (**5e**).* Red solid. ^1H NMR (300 MHz, $CDCl_3$): δ 8.08 (d, J = 7.6 Hz, 1H), 8.02 (d, J = 7.6 Hz, 1H), 7.70 (t, J = 7.5 Hz, 1H), 7.58 (t, J = 7.2 Hz, 1H), 5.87 (brs, 1H), 5.71 (s, 1H), 3.15 (m, 2H), 1.67 (m, 2H), 1.33 (m, 6H), 0.88 (t, J = 5.9 Hz, 3H).

*2-((3-Phenylpropyl)amino)naphthalene-1,4-dione (**5f**).* Red solid. ^1H NMR (300 MHz, $CDCl_3$): δ 8.08 (d, J = 7.7 Hz, 1H), 8.02 (d, J = 7.6 Hz, 1H), 7.70 (t, J = 7.5 Hz, 1H), 7.59 (t, J = 7.5 Hz, 1H), 7.28 (m, 2H), 7.18 (m, 3H), 5.88 (brs, 1H), 5.68 (s, 1H), 3.17 (m, 2H), 2.72 (t, J = 7.5 Hz, 2H), 2.01 (m, 2H).

*2-(Isobutylamino)naphthalene-1,4-dione (**5g**).* Red solid. ^1H NMR (300 MHz, $CDCl_3$): δ 8.08 (d, J = 7.6 Hz, 1H), 8.02 (d, J = 7.6 Hz, 1H), 7.70 (td, J = 7.6, 1.3 Hz, 1H), 7.59 (td, J = 7.6, 1.2 Hz, 1H), 5.97 (brs, 1H), 5.71 (s, 1H), 2.99 (m, 2H), 1.98 (m, 1H), 0.99 (d, J = 6.7 Hz, 6H).

*2-(Neopentylamino)naphthalene-1,4-dione (**5h**).* Red solid. ^1H NMR (300 MHz, $CDCl_3$): δ 8.08 (d, J = 7.4 Hz, 1H), 8.03 (d, J = 7.5 Hz, 1H), 7.71 (t, J = 7.1 Hz, 1H), 7.59 (t, J = 7.1 Hz, 1H), 5.99 (brs, 1H), 5.75 (s, 1H), 2.94 (d, J = 6.2 Hz, 2H), 1.01 (s, 9H).

*2-((Cyclopropylmethyl)amino)naphthalene-1,4-dione (**5i**).* Red solid. ^1H NMR (300 MHz, $CDCl_3$): δ 8.07 (d, J = 7.6 Hz, 1H), 8.03 (d, J = 7.6 Hz, 1H), 7.70 (t, J = 7.5 Hz, 1H), 7.59 (t, J = 7.5 Hz, 1H), 5.98 (brs, 1H), 5.68 (s, 1H), 3.00 (m, 2H), 1.11 (m, 1H), 0.62 (m, 2H), 0.29 (m, 2H).

*2-((Adamantan-1-ylmethyl)amino)naphthalene-1,4-dione (**5j**).* Red solid. ^1H NMR (300 MHz, $CDCl_3$): δ 8.06 (d, J = 7.6 Hz, 1H), 8.01 (d, J = 7.6 Hz, 1H), 7.69 (t, J = 7.5 Hz, 1H), 7.57 (t, J = 7.5 Hz, 1H), 6.01 (brs, 1H), 5.74 (s, 1H), 2.83 (d, J = 6.3 Hz, 2H), 1.99 (m, 3H), 1.67 (m, 6H), 1.56 (m, 6H).

*tert-Butyl (3-((1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)propyl)(methyl)carbamate (**5k**).* Red solid. ^1H NMR (300 MHz, $CDCl_3$): δ 8.07 (d, J = 7.7 Hz, 1H), 8.02 (d, J = 7.7 Hz, 1H), 7.69 (t, J = 7.5 Hz, 1H), 7.58 (t, J = 7.5 Hz, 1H), 6.47 (brs, 0.44H), 5.92 (brs, 0.29H), 5.70 (s, 1H), 3.31 (t, J = 6.5 Hz, 2H), 3.19 (m, 2H), 2.84 (s, 3H), 1.83 (m, 2H), 1.45 (s, 9H).

*2-((2-(Tetrahydro-2H-pyran-4-yl)ethyl)amino)naphthalene-1,4-dione (**5l**).* Red solid. ^1H NMR (300 MHz, $CDCl_3$): δ 8.08 (d, J = 7.5 Hz, 1H), 8.03 (d, J = 7.5 Hz, 1H), 7.71 (t, J = 7.4 Hz, 1H), 7.60 (t, J = 7.5 Hz, 1H), 5.83 (brs, 1H), 5.71 (s, 1H), 3.96 (m, 2H), 3.37 (m, 2H), 3.21 (m, 2H), 1.63 (m, 5H), 1.34 (m, 2H).

*8-Methoxy-2-(propylamino)naphthalene-1,4-dione (**5m**).* Red solid. ^1H NMR (300 MHz, $CDCl_3$): δ 7.74 (d, J = 7.4 Hz, 1H), 7.61 (t, J = 7.8 Hz, 1H), 7.13 (d, J = 8.2 Hz, 1H), 6.02 (brs, 1H), 5.62 (s, 1H), 3.96 (s, 3H), 3.09 (m, 2H), 1.66 (m, 2H), 0.96 (t, J = 7.2 Hz, 3H).

*8-(Benzyloxy)-2-(propylamino)naphthalene-1,4-dione (**5n**).* Red solid. ^1H NMR (300 MHz, $CDCl_3$): δ 7.78 (d, J = 7.6 Hz, 1H), 7.61 (t, J = 8.2 Hz, 1H), 7.55 (d, J = 7.6 Hz, 2H), 7.40 (t, J = 7.5 Hz, 2H), 7.32 (t, J = 7.8 Hz, 1H), 7.19 (d, J = 8.4 Hz, 1H), 6.08 (brs, 1H), 5.66

dx.doi.org/10.1021/jo500572u | J. Org. Chem. 2014, 79, 4553–4560

(s, 1H), 5.26 (s, 2H), 3.11 (m, 2H), 1.71 (m, 2H), 0.99 (t, J = 7.4 Hz, 3H).

*2-(Propylamino)anthracene-1,4-dione (**5o**).* Red solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.56 (s, 2H), 7.98 (d, J = 7.4 Hz, 2H), 7.59 (m, 2H), 6.00 (brs, 1H), 5.84 (s, 1H), 3.16 (m, 2H), 1.72 (m, 2H), 1.02 (t, J = 7.3 Hz, 3H).

*2-Methyl-3-(propylamino)naphthalene-1,4-dione (**5p**).* Red solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.04 (d, J = 7.6 Hz, 1H), 7.95 (d, J = 7.8 Hz, 1H), 7.64 (t, J = 7.5 Hz, 1H), 7.53 (t, J = 7.5 Hz, 1H), 5.72 (brs, 1H), 3.48 (m, 2H), 2.20 (s, 3H), 1.64 (m, 2H), 0.97 (t, J = 7.4 Hz, 3H).

*2-Phenyl-3-(propylamino)naphthalene-1,4-dione (**5q**).* Red solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.11 (dd, J = 7.7, 0.8 Hz, 1H), 8.06 (m, 1H), 7.71 (td, J = 7.5, 1.3 Hz, 1H), 7.60 (td, J = 7.5, 1.3 Hz, 1H), 7.33 (m, 5H), 5.95 (brs, 1H), 2.55 (m, 2H), 1.35 (m, 2H), 0.69 (t, J = 7.4 Hz, 3H).

*5-Methoxy-2-(propylamino)naphthalene-1,4-dione (**5r**).* Red solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.68 (d, J = 7.6 Hz, 1H), 7.51 (t, J = 8.0 Hz, 1H), 7.26 (d, J = 8.8 Hz, 1H), 5.61 (s, 1H), 5.57 (brs, 1H), 3.94 (s, 3H), 3.06 (m, 2H), 1.65 (m, 2H), 0.96 (t, J = 7.4 Hz, 3H).

*2-(Pyrrolidin-1-yl)naphthalene-1,4-dione (**5s**).* Red solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.99 (d, J = 7.4 Hz, 1H), 7.92 (d, J = 7.4 Hz, 1H), 7.62 (t, J = 6.9 Hz, 1H), 7.52 (t, J = 7.3 Hz, 1H), 5.65 (s, 1H), 3.83 (m, 2H), 3.38 (m, 2H), 1.93 (m, 4H).

General Procedure for Synthesis of Naphthoxazole Derivatives. A solution of 2-amino-1,4-naphthoquinones **5** (0.4 mmol), alkynes **6** (0.6 mmol), $[Cp^*RhCl_2]_2$ (0.05 equiv), $AgSbF_6$ (0.2 equiv), and $Cu(OAc)_2{\cdot}H_2O$ (0.8 mmol) in *t*-AmOH (2 mL) was stirred in sealed glass tubes (10 mL) at 120 °C for 6 h. The reaction was then cooled to room temperature, diluted with EtOAc, and filtered. The filtrate was concentrated *in vacuo* and purified by column chromatography using petroleum ether/ethyl acetate (v/v = 2:1) to give the oxazole derivatives **7**.

*9-Ethyl-4,5-diphenylbenzo[4,5]chromeno[7,6-d]oxazole (**7aa**).* Yellow solid, 113 mg (73%). mp = 153−155 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.60 (d, J = 8.4 Hz, 1H), 7.33 (m, 5H), 7.20 (m, 7H), 6.49 (d, J = 7.4 Hz, 1H), 3.03 (q, J = 7.6 Hz, 2H), 1.50 (t, J = 7.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 168.2, 150.0 (2), 140.7, 138.6, 135.3, 134.0, 133.2, 131.1, 129.1, 129.0, 128.7, 128.6, 127.7, 127.6, 120.6, 120.1, 116.3, 116.1, 115.8, 98.5, 22.4, 11.1. EI-MS (m/z): 389 (M^+). HRMS (EI): calcd for $C_{27}H_{19}NO_2$ (M^+), 389.1416; found, 389.1418.

*9-Ethyl-4,5-di-p-tolylbenzo[4,5]chromeno[7,6-d]oxazole (**7ab**).* Yellow solid, 110 mg (66%). mp = 133−135 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, J = 8.3 Hz, 1H), 7.27 (m, 5H), 7.17 (m, 3H), 7.03 (d, J = 8.1 Hz, 2H), 6.53 (m, 1H), 3.06 (q, J = 7.6 Hz, 2H), 2.42 (s, 3H), 2.32 (s, 3H), 1.53 (t, J = 7.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.1, 150.0, 149.9, 140.5, 138.5, 138.4, 137.1, 133.5, 132.3, 131.2, 130.9, 129.8, 128.8, 128.6, 128.4, 120.5, 120.0, 115.8, 115.6, 98.3, 22.3, 21.3 (2), 11.1. EI-MS (m/z): 417 (M^+). HRMS (EI): calcd for $C_{29}H_{23}NO_2$ (M^+), 417.1729; found, 417.1734.

*4,5-Bis(4-chlorophenyl)-9-ethylbenzo[4,5]chromeno[7,6-d]oxazole (**7ac**).* Yellow solid, 114 mg (64%). mp = 162−164 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.61 (d, J = 8.4 Hz, 1H), 7.36 (d, J = 8.3 Hz, 2H), 7.24 (m, 2H), 7.18 (m, 4H), 7.14 (m, 2H), 6.43 (d, J = 7.4 Hz, 1H), 3.02 (q, J = 7.6 Hz, 2H), 1.49 (t, J = 7.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.3, 149.5, 149.1, 140.7, 138.6, 134.7, 133.8, 133.5, 132.4, 132.1, 130.2, 129.6, 128.6, 128.1, 120.3, 120.0, 116.6, 115.7, 115.5, 98.7, 22.3, 11.1. EI-MS (m/z): 457 (M^+). HRMS (EI): calcd for $C_{27}H_{17}Cl_2NO_2$ (M^+), 457.0636; found, 457.0633.

*9-Ethyl-4,5-bis(4-fluorophenyl)benzo[4,5]chromeno[7,6-d]oxazole (**7ad**).* Yellow solid, 102 mg (60%). mp = 155−157 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.61 (d, J = 8.1 Hz, 1H), 7.27 (m, 3H), 7.18 (d, J = 5.5 Hz, 2H), 7.14 (s, 1H), 7.08 (t, J = 8.2 Hz, 2H), 6.88 (t, J = 8.5 Hz, 2H), 6.45 (d, J = 7.2 Hz, 1H), 3.02 (q, J = 7.5 Hz, 2H), 1.49 (t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 167.8, 162.1 (d, J = 250 Hz), 161.8 (d, J = 248 Hz), 149.2, 148.9, 140.2, 138.2, 132.4, 132.3 (d, J = 8.0 Hz), 130.5 (d, J = 3.6 Hz), 130.4 (d, J = 8.3 Hz), 129.5 (d, J = 3.2 Hz), 128.2, 119.9, 119.6, 115.9, 115.9 (d, J = 21.4 Hz), 115.1, 114.8, 114.4 (d, J = 21.7 Hz), 98.2, 21.9, 10.6. EI-MS (m/z): 425 (M^+). HRMS (EI): calcd for $C_{27}H_{17}F_2NO_2$ (M^+), 425.1227; found, 425.1226.

*9-Ethyl-4,5-bis(4-ethylphenyl)benzo[4,5]chromeno[7,6-d]oxazole (**7ae**).* Yellow solid, 108 mg (61%). mp = 141−143 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.58 (d, J = 7.8 Hz, 1H), 7.25 (m, 4H), 7.19 (s, 1H), 7.15 (m, 3H), 7.01 (d, J = 8.2 Hz, 2H), 6.50 (d, J = 7.0 Hz, 1H), 3.02 (q, J = 7.6 Hz, 2H), 2.68 (q, J = 7.6 Hz, 2H), 2.57 (q, J = 7.6 Hz, 2H), 1.49 (t, J = 7.6 Hz, 3H), 1.28 (t, J = 7.6 Hz, 3H), 1.17 (t, J = 7.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.1, 150.0, 149.9, 144.7, 143.5, 138.5, 133.6, 132.5, 131.4, 130.9, 128.8, 128.7, 128.6, 127.2, 120.5, 120.1, 115.8, 115.7, 98.3, 28.6 (2), 22.3, 15.4, 15.2, 11.1. EI-MS (m/z): 445 (M^+). HRMS (EI): calcd for $C_{31}H_{27}NO_2$ (M^+), 445.2042; found, 445.2040.

*9-Ethyl-4,5-bis(4-methoxyphenyl)benzo[4,5]chromeno[7,6-d]oxazole (**7af**).* Yellow solid, 86 mg (48%). mp = 150−151 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.57 (d, J = 8.3 Hz, 1H), 7.25 (m, 3H), 7.15 (m, 3H), 6.92 (d, J = 8.6 Hz, 2H), 6.71 (d, J = 8.8 Hz, 2H), 6.49 (d, J = 7.4 Hz, 1H), 3.82 (s, 3H), 3.75 (s, 3H), 3.02 (q, J = 7.6 Hz, 2H), 1.49 (t, J = 7.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.1, 159.5, 158.8, 150.0, 149.8, 140.5, 138.5, 133.7, 132.2, 130.3, 128.7, 127.6, 126.5, 120.4, 120.0, 115.7, 115.4, 114.7, 114.6, 113.1, 98.2, 55.2 (2), 22.3, 11.1. EI-MS (m/z): 449 (M^+). HRMS (EI): calcd for $C_{29}H_{23}NO_4$ (M^+), 449.1627; found, 449.1631.

*9-Ethyl-4,5-bis(4-(trifluoromethyl)phenyl)benzo[4,5]chromeno-[7,6-d]oxazole (**7ag**).* Yellow solid, 149 mg (71%). mp = 181−183 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, J = 8.1 Hz, 3H), 7.50 (d, J = 8.3 Hz, 2H), 7.42 (d, J = 8.2 Hz, 4H), 7.32 (t, J = 7.9 Hz, 1H), 7.21 (s, 1H), 6.45 (d, J = 7.3 Hz, 1H), 3.07 (q, J = 7.6 Hz, 2H), 1.54 (t, J = 7.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.5, 149.4, 149.0, 140.9, 138.7, 137.0, 132.0, 131.5, 130.7 (q, J = 32.8 Hz), 130.3 (q, J = 32.5 Hz), 129.3, 128.7, 126.4 (d, J = 3.6 Hz), 125.0 (d, J = 3.7 Hz), 124.0 (q, J = 273.2 Hz), 123.7 (q, J = 273.6 Hz), 120.4, 120.1, 117.1, 116.5, 116.0, 99.1, 22.4, 11.1. EI-MS (m/z): 525 (M^+). HRMS (EI): calcd for $C_{29}H_{17}F_6NO_2$ (M^+), 525.1163; found, 525.1159.

*9-Ethyl-4,5-di(thiophen-2-yl)benzo[4,5]chromeno[7,6-d]oxazole (**7ah**).* Yellow solid, 83 mg (52%). mp = 205−206 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.59 (t, J = 5.6 Hz, 2H), 7.26 (m, 3H), 7.19 (s, 2H), 7.07 (m, 1H), 6.94 (m, 1H), 6.48 (d, J = 7.3 Hz, 1H), 3.02 (q, J = 7.6 Hz, 2H), 1.49 (t, J = 7.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.2, 149.1, 146.8, 140.8, 138.5, 135.6, 135.2, 133.5, 129.9, 128.8, 128.7, 128.4, 128.3, 128.2, 126.7, 119.8, 119.7, 116.2, 116.1, 107.2, 98.8, 22.3, 11.1. EI-MS (m/z): 401 (M^+). HRMS (EI): calcd for $C_{23}H_{15}NO_2S_2$ (M^+), 401.0544; found, 401.0536.

*9-Ethyl-4,5-dipropylbenzo[4,5]chromeno[7,6-d]oxazole (**7ai**).* Yellow solid, 86 mg (67%). mp = 72−73 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.55 (d, J = 8.3 Hz, 1H), 7.36 (m, 1H), 6.99 (s, 1H), 6.79 (d, J = 7.3 Hz, 1H), 2.99 (q, J = 7.6 Hz, 2H), 2.40 (m, 4H), 1.70 (m, 2H), 1.56 (m, 2H), 1.46 (t, J = 7.6 Hz, 3H), 1.01 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 167.9, 152.9, 150.0, 140.3, 138.3, 132.1, 128.7, 120.8, 120.2, 114.9, 112.6, 110.6, 97.7, 32.7, 28.4, 22.3, 21.3, 21.1, 14.3, 13.9, 11.1. EI-MS (m/z): 321 (M^+). HRMS (EI): calcd for $C_{21}H_{23}NO_2$ (M^+), 321.1729; found, 321.1727.

*4-Butyl-9-ethyl-5-phenylbenzo[4,5]chromeno[7,6-d]oxazole (**7aj**).* Yellow solid, 92 mg (63%). mp = 88−90 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64 (d, J = 8.3 Hz, 1H), 7.55 (m, 2H), 7.44 (m, 4H), 7.06 (s, 1H), 6.93 (d, J = 7.3 Hz, 1H), 3.01 (q, J = 7.6 Hz, 2H), 2.42 (m, 2H), 1.59 (m, 2H), 1.48 (t, J = 7.6 Hz, 3H), 1.33 (m, 2H), 0.86 (t, J = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 168.1, 150.6, 150.0, 140.5, 138.5, 134.8, 131.8, 129.0, 128.9, 128.7, 128.3, 120.9, 120.2, 115.9, 113.7, 112.8, 98.2, 30.3, 26.8, 22.8, 22.3, 13.8, 11.1. EI-MS (m/z): 369 (M^+). HRMS (EI): calcd for $C_{25}H_{23}NO_2$ (M^+), 369.1729; found, 369.1723.

*9-Ethyl-4-methyl-5-propylbenzo[4,5]chromeno[7,6-d]oxazole (**7ak**).* Yellow solid, 44 mg (38%). mp = 75−77 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.57 (dd, J = 8.3, 0.7 Hz, 1H), 7.39 (m, 1H), 7.02 (s, 1H), 6.75 (d, J = 6.6 Hz, 1H), 3.00 (q, J = 7.6 Hz, 2H), 2.44 (m, 2H), 1.94 (s, 3H), 1.72 (m, 2H), 1.47 (t, J = 7.6 Hz, 3H), 1.00 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 167.9, 152.5, 150.0, 140.3, 138.4, 133.0, 128.8, 120.3, 119.9, 115.1, 112.5, 106.1, 97.8, 32.9, 22.4,

dx.doi.org/10.1021/jo500572u | J. Org. Chem. 2014, 79, 4553−4560

21.1, 13.8, 12.3, 11.2. EI-MS (m/z): 293 (M^+). HRMS (EI): calcd for $C_{19}H_{19}NO_2$ (M^+), 293.1416; found, 293.1416.

*9-Ethyl-5-methyl-4-propylbenzo[4,5]chromeno[7,6-d]oxazole (**7ak'**).* Yellow solid, 43 mg (37%). mp = 86−88 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, J = 8.2 Hz, 1H), 7.40 (m, 1H), 7.03 (s, 1H), 6.81 (d, J = 7.3 Hz, 1H), 3.03 (q, J = 7.6 Hz, 2H), 2.41 (m, 2H), 2.16 (s, 3H), 1.60 (m, 2H), 1.51 (t, J = 7.6 Hz, 3H), 1.04 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 167.9, 149.9, 149.4, 140.4, 138.3, 132.0, 128.7, 120.8, 120.2, 114.9, 112.3, 110.6, 97.8, 28.6, 22.3, 20.8, 17.1, 14.2, 11.1. EI-MS (m/z): 293 (M^+). HRMS (EI): calcd for $C_{19}H_{19}NO_2$ (M^+), 293.1416; found, 293.1415.

*4,5-Diphenyl-9-propylbenzo[4,5]chromeno[7,6-d]oxazole (**7ba**).* Yellow solid, 96 mg (60%). mp = 123−125 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.60 (d, J = 8.4 Hz, 1H), 7.32 (m, 5H), 7.23 (m, 6H), 7.18 (s, 1H), 6.49 (d, J = 7.4 Hz, 1H), 2.97 (t, J = 7.5 Hz, 2H), 1.98 (m, 2H), 1.08 (t, J = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 167.2, 150.0, 149.9, 140.6, 138.6, 135.3, 134.0, 133.2, 131.1, 129.1, 129.0, 128.7, 128.6, 127.7, 127.6, 120.6, 120.1, 116.3, 116.2, 115.8, 98.5, 30.7, 20.5, 13.9. EI-MS (m/z): 403 (M^+). HRMS (EI): calcd for $C_{28}H_{21}NO_2$ (M^+), 403.1572; found, 403.1563.

*9-Butyl-4,5-diphenylbenzo[4,5]chromeno[7,6-d]oxazole (**7ca**).* Yellow solid, 105 mg (63%). mp = 107−108 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.61 (d, J = 8.3 Hz, 1H), 7.28 (m, 12H), 6.49 (d, J = 7.4 Hz, 1H), 2.99 (t, J = 7.6 Hz, 2H), 1.92 (m, 2H), 1.49 (m, 2H), 0.99 (t, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 167.4, 150.0, 149.9, 140.6, 138.6, 135.3, 134.0, 133.1, 131.1, 129.1, 128.9, 128.6, 128.5, 127.7, 127.6, 120.5, 120.1, 116.2, 116.1, 115.7, 98.5, 29.1, 28.5, 22.3, 13.7. EI-MS (m/z): 417 (M^+). HRMS (EI): calcd for $C_{29}H_{23}NO_2$ (M^+), 417.1729; found, 417.1735.

*9-Isobutyl-4,5-diphenylbenzo[4,5]chromeno[7,6-d]oxazole (**7da**).* Yellow solid, 90 mg (54%). mp = 125−127 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.61 (d, J = 8.4 Hz, 1H), 7.33 (m, 5H), 7.25 (m, 3H), 7.18 (m, 4H), 6.50 (d, J = 7.4 Hz, 1H), 2.87 (d, J = 7.2 Hz, 2H), 2.35 (m, 1H), 1.07 (d, J = 6.7 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 166.7, 150.0, 149.9, 140.6, 138.6, 135.3, 134.0, 133.2, 131.1, 129.1, 129.0, 128.6, 128.5, 127.7, 127.6, 120.6, 120.1, 116.2 (2), 115.7, 98.5, 37.7, 27.7, 22.5. EI-MS (m/z): 417 (M^+). HRMS (EI): calcd for $C_{29}H_{23}NO_2$ (M^+), 417.1729; found, 417.1721.

*9-Pentyl-4,5-diphenylbenzo[4,5]chromeno[7,6-d]oxazole (**7ea**).* Yellow solid, 115 mg (67%). mp = 90−91 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.61 (d, J = 8.3 Hz, 1H), 7.26 (m, 12H), 6.49 (d, J = 7.3 Hz, 1H), 2.98 (t, J = 7.7 Hz, 2H), 1.94 (m, 2H), 1.42 (m, 4H), 0.93 (t, J = 6.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 167.4, 150.0, 149.9, 140.6, 138.6, 135.3, 134.0, 133.2, 131.1, 129.1, 129.0, 128.6, 128.5, 127.7, 127.6, 120.5, 120.1, 116.2, 116.1, 115.7, 98.5, 31.4, 28.8, 26.7, 22.3, 13.9. EI-MS (m/z): 431 (M^+). HRMS (EI): calcd for $C_{30}H_{25}NO_2$ (M^+), 431.1885; found, 431.1894.

*9-Phenethyl-4,5-diphenylbenzo[4,5]chromeno[7,6-d]oxazole (**7fa**).* Yellow solid, 141 mg (76%). mp = 163−165 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.61 (d, J = 8.3 Hz, 1H), 7.28 (m, 17H), 6.51 (d, J = 7.3 Hz, 1H), 3.29 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 166.3, 150.0, 140.6, 140.2, 138.5, 135.2, 134.0, 133.2, 131.1, 129.1, 128.9, 128.7, 128.6, 128.5, 128.3, 127.7, 127.6, 126.5, 120.6, 120.1, 116.2, 116.1, 115.8, 98.5, 33.1, 30.7. EI-MS (m/z): 465 (M^+). HRMS (EI): calcd for $C_{33}H_{23}NO_2$ (M^+), 465.1729; found, 465.1728.

*9-Isopropyl-4,5-diphenylbenzo[4,5]chromeno[7,6-d]oxazole (**7ga**).* Yellow solid, 153 mg (95%). mp = 180−181 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, J = 8.3 Hz, 1H), 7.40 (m, 3H), 7.34 (m, 2H), 7.29 (m, 3H), 7.23 (m, 4H), 6.54 (d, J = 7.3 Hz, 1H), 3.35 (m, 1H), 1.55 (d, J = 7.0 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 171.4, 150.0, 149.9, 140.6, 138.5, 135.3, 134.1, 133.2, 131.1, 129.1, 129.0, 128.6 (2), 127.7, 127.6, 120.6, 120.2, 116.3, 116.2, 115.8, 98.6, 29.1, 20.6. EI-MS (m/z): 403 (M^+). HRMS (EI): calcd for $C_{28}H_{21}NO_2$ (M^+), 403.1572; found, 403.1566.

*9-(tert-Butyl)-4,5-diphenylbenzo[4,5]chromeno[7,6-d]oxazole (**7ha**).* Yellow solid, 123 mg (74%). mp = 186−188 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, J = 8.2 Hz, 1H), 7.40 (m, 3H), 7.35 (m, 2H), 7.29 (m, 3H), 7.22 (m, 4H), 6.54 (d, J = 7.3 Hz, 1H), 1.58 (s, 9H). ^{13}C NMR (126 MHz, CDCl3): δ 173.6, 150.0, 149.9, 140.6, 138.5, 135.4, 134.1, 133.2, 131.2, 129.1, 129.0, 128.6 (2), 127.7, 127.6, 120.6, 120.2, 116.3, 116.2, 115.7, 98.7, 34.4, 28.7. EI-MS (m/z): 417 (M^+). HRMS (EI): calcd for $C_{29}H_{23}NO_2$ (M^+), 417.1729; found, 417.1728.

*9-Cyclopropyl-4,5-diphenylbenzo[4,5]chromeno[7,6-d]oxazole (**7ia**).* Yellow solid, 149 mg (93%). mp = 203−205 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, J = 8.3 Hz, 1H), 7.39 (m, 3H), 7.34 (m, 2H), 7.28 (m, 3H), 7.21 (m, 3H), 7.14 (s, 1H), 6.51 (d, J = 7.3 Hz, 1H), 2.30 (m, 1H), 1.35 (m, 2H), 1.23 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 168.6, 150.0, 140.2, 138.9, 135.3, 134.1, 133.2, 131.1, 129.1, 129.0, 128.6, 128.5, 127.7, 127.6, 120.3, 119.9, 116.3, 116.0, 115.5, 98.3, 9.6, 9.3. EI-MS (m/z): 401 (M^+). HRMS (EI): calcd for $C_{28}H_{19}NO_2$ (M^+), 401.1416; found, 401.1414.

*9-((3r,5r,7r)-Adamantan-1-yl)-4,5-diphenylbenzo[4,5]chromeno-[7,6-d]oxazole (**7ja**).* Yellow solid, 126 mg (64%). mp = 141−143 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, J = 8.3 Hz, 1H), 7.40 (m, 3H), 7.35 (m, 2H), 7.29 (m, 3H), 7.22 (m, 4H), 6.52 (d, J = 7.3 Hz, 1H), 2.26 (m, 6H), 2.19 (s, 3H), 1.88 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 173.1, 150.0, 149.8, 140.3, 138.4, 135.3, 134.0, 133.1, 131.1, 129.1, 129.0, 128.5, 127.7, 127.6, 120.5, 120.1, 116.2, 115.6, 98.6, 40.4, 36.5, 36.3, 28.0. EI-MS (m/z): 495 (M^+). HRMS (EI): calcd for $C_{35}H_{29}NO_2$ (M^+), 495.2198; found, 495.2197.

*tert-Butyl(2-(4,5-diphenylbenzo[4,5]chromeno[7,6-d]oxazol-9-yl)ethyl)(methyl)carbamate (**7ka**).* Yellow solid, 93 mg (45%). mp = 143−145 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, J = 8.3 Hz, 1H), 7.39 (m, 3H), 7.34 (m, 2H), 7.29 (m, 3H), 7.23 (m, 3H), 7.19 (s, 1H), 6.55 (d, J = 7.4 Hz, 1H), 3.81 (t, J = 6.8 Hz, 2H), 3.24 (m, 2H), 2.93 (m, 3H), 1.43 (m, 9H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 164.6, 155.4, 150.1, 150.0, 140.8, 138.6, 135.3, 134.0, 133.2, 131.1, 129.1, 129.0, 128.8, 128.6, 127.7 (2), 120.7, 120.2, 116.3, 116.2, 116.0, 98.5, 79.8, 47.0, 34.4, 29.7, 28.4. EI-MS (m/z): 518 (M^+). HRMS (EI): calcd for $C_{33}H_{30}N_2O_4$ (M^+), 518.2206; found, 518.2205.

*4,5-Diphenyl-9-((tetrahydro-2H-pyran-4-yl)methyl)benzo[4,5]-chromeno[7,6-d]oxazole (**7la**).* Yellow solid, 150 mg (82%). mp = 140−142 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.61 (d, J = 7.7 Hz, 1H), 7.36 (m, 3H), 7.30 (m, 3H), 7.22 (m, 5H), 7.15 (s, 1H), 6.51 (d, J = 6.9 Hz, 1H), 3.98 (dd, J = 11.4, 3.0 Hz, 2H), 3.44 (td, J = 11.7, 1.6 Hz, 2H), 2.94 (d, J = 7.1 Hz, 2H), 2.25 (m, 1H), 1.74 (d, J = 11.3 Hz, 2H), 1.50 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 167.0, 151.5, 142.1, 140.0, 136.7, 135.4, 134.6, 132.5, 130.6, 130.4, 130.2, 130.0, 129.2, 129.1, 122.1, 121.5, 117.7, 117.6, 117.3, 99.9, 69.2, 37.4, 35.5, 34.3. EI-MS (m/z): 459 (M^+). HRMS (EI): calcd for $C_{31}H_{25}NO_3$ (M^+), 459.1834; found, 459.1833.

*9-Ethyl-1-methoxy-4,5-diphenylbenzo[4,5]chromeno[7,6-d]-oxazole (**7ma**).* Yellow solid, 78 mg (47%). mp = 157−158 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.29 (m, 8H), 7.17 (m, 3H), 6.67 (d, J = 8.2 Hz, 1H), 6.42 (d, J = 8.1 Hz, 1H), 3.98 (s, 3H), 3.05 (q, J = 7.6 Hz, 2H), 1.50 (t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 168.6, 151.1, 150.0, 147.6, 139.9, 139.6, 135.6, 134.1, 131.1, 129.1, 128.8, 128.2, 127.7, 127.6, 125.8, 122.0, 116.3, 116.2, 113.0, 107.2, 99.9, 55.9, 22.3, 11.1. EI-MS (m/z): 419 (M^+). HRMS (EI): calcd for $C_{28}H_{21}NO_3$ (M^+), 419.1521; found, 419.1521.

*1-(Benzyloxy)-9-ethyl-4,5-diphenylbenzo[4,5]chromeno[7,6-d]-oxazole (**7na**).* Yellow solid, 91 mg (46%). mp = 179−181 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64 (d, J = 7.3 Hz, 2H), 7.39 (m, 6H), 7.29 (m, 2H), 7.24 (m, 2H), 7.19 (m, 4H), 6.75 (d, J = 8.2 Hz, 1H), 6.41 (d, J = 8.2 Hz, 1H), 5.24 (s, 2H), 3.04 (q, J = 7.5 Hz, 2H), 1.49 (t, J = 7.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 168.4, 150.0 (2), 147.8, 140.0, 139.6, 137.0, 135.6, 134.1, 131.1, 129.1, 128.8, 128.5, 128.3, 127.8, 127.7, 127.6, 126.9, 126.1, 122.0, 116.2, 113.4, 108.7, 99.9, 70.3, 22.4, 11.0. EI-MS (m/z): 495 (M^+). HRMS (EI): calcd for $C_{34}H_{25}NO_3$ (M^+), 495.1834; found, 495.1839.

*10-Ethyl-5,6-diphenylnaphtho[1′,2′,3′:4,5]chromeno[7,6-d]-oxazole (**7oa**).* Red solid, 151 mg (86%). mp = 171−173 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.19 (s, 1H), 7.79 (d, J = 8.1 Hz, 1H), 7.27 (m, 3H), 7.22 (m, 6H), 7.16 (m, 2H), 7.05 (m, 2H), 6.77 (m, 1H), 3.06 (q, J = 7.6 Hz, 2H), 1.52 (t, J = 7.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$: δ 167.8, 153.2, 150.8, 140.3, 138.9, 137.3, 134.6 (2), 131.4, 129.3, 128.9, 128.6, 128.3, 127.7, 127.4, 126.9, 126.0, 123.7, 122.9, 121.3, 118.8, 117.5, 115.9, 96.5, 22.4, 11.3. EI-MS (m/z): 439 (M^+). HRMS (EI): calcd for $C_{31}H_{21}NO_2$ (M^+), 439.1572; found, 439.1570.

dx.doi.org/10.1021/jo500572u | J. Org. Chem. 2014, 79, 4553−4560

*9-Ethyl-7-methyl-4,5-diphenylbenzo[4,5]chromeno[7,6-d]-oxazole (**7pa**).* Yellow solid, 112 mg (70%). mp = 168−169 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.57 (d, J = 8.4 Hz, 1H), 7.36 (m, 5H), 7.26 (d, J = 8.5 Hz, 2H), 7.19 (m, 4H), 6.45 (d, J = 7.3 Hz, 1H), 3.04 (q, J = 7.6 Hz, 2H), 2.57 (s, 3H), 1.49 (t, J = 7.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 167.6, 149.5, 146.2, 139.9, 138.8, 135.5, 134.3, 132.7, 131.1, 129.1, 128.7, 128.3, 127.6, 127.5, 127.4, 120.3, 118.1, 116.1, 116.0, 115.6, 108.1, 22.4, 11.4, 9.9. EI-MS (m/z): 403 (M^+). HRMS (EI): calcd for $C_{28}H_{21}NO_2$ (M^+), 403.1572; found, 403.1573.

*9-Ethyl-4,5,7-triphenylbenzo[4,5]chromeno[7,6-d]oxazole (**7qa**).* Yellow solid, 165 mg (89%). mp = 197−199 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.87 (d, J = 8.0 Hz, 2H), 7.65 (d, J = 8.3 Hz, 1H), 7.48 (m, 2H), 7.38 (m, 4H), 7.27 (m, 3H), 7.19 (d, J = 7.9 Hz, 2H), 7.10 (m, 3H), 6.52 (d, J = 7.4 Hz, 1H), 3.03 (q, J = 7.6 Hz, 2H), 1.47 (t, J = 7.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 167.8, 149.4, 145.5, 140.6, 137.8, 135.5, 133.7, 133.6, 133.0, 131.1, 130.6, 129.3, 128.8, 128.4, 128.0, 127.7, 127.5, 127.4, 120.6, 119.4, 116.4, 116.2, 116.1, 112.6, 22.5, 11.5. EI-MS (m/z): 465 (M^+). HRMS (EI): calcd for $C_{33}H_{23}NO_2$ (M^+), 465.1729; found, 465.1727.

*1-(4,5-Diphenylbenzo[4,5]chromeno[7,6-d]oxazol-9-yl)ethyl Acetate (**8aa**).* Yellow solid, 21 mg (12%). mp = 133−135 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.65 (d, J = 8.3 Hz, 1H), 7.35 (m, 5H), 7.23 (m, 7H), 6.55 (d, J = 7.5 Hz, 1H), 6.18 (q, J = 6.7 Hz, 1H), 2.19 (s, 3H), 1.80 (d, J = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 170.0, 164.0, 150.4, 150.1, 140.9, 138.2, 135.2, 133.9, 133.2, 131.1, 129.2 129.0, 128.9, 128.6, 127.7 (2), 121.2, 120.3, 116.4, 116.3, 98.7, 65.4, 21.0, 18.6. EI-MS (m/z): 447 (M^+). HRMS (EI): calcd for $C_{29}H_{21}NO_4$ (M^+), 447.1471; found, 447.1473.

Deuterium Labeling Experiments. *H/D Scrambling of **5a** and **5p** in the Absence of Alkyne.* A solution of 2-amino-1,4-naphthoquinones **5a** or **5p** (0.2 mmol), $[Cp^*RhCl_2]_2$ (0.05 equiv), $AgSbF_6$ (0.2 equiv), and $Cu(OAc)_2{\cdot}H_2O$ (0.4 mmol) in CD_3OD (1 mL) was stirred in sealed tubes at 120 °C for 4 h. The reaction was cooled to room temperature, concentrated *in vacuo*, and purified by column chromatography to give [D]-**5a** or [D]-**5p**.

*Oxidative Annulations of **5a** in the Presence of CD_3OD.* A solution of **5a** (0.2 mmol), **6i** (0.3 mmol), $[Cp^*RhCl_2]_2$ (0.05 equiv), $AgSbF_6$ (0.2 equiv), and $Cu(OAc)_2{\cdot}H_2O$ (0.4 mmol) in CD_3OD (1 mL) was stirred in sealed tubes at 120 °C for 4 h. The reaction was cooled to room temperature, concentrated *in vacuo*, and purified by column chromatography to give [D]-**7ai** and [D]-**5a**.

Kinetic Isotope Effect Experiments. A solution of 2-amino-1,4-naphthoquinones **5p** or [D_5]-**5p** (0.4 mmol), alkynes **2a** (0.6 mmol), $[Cp^*RhCl_2]_2$ (0.05 equiv), $AgSbF_6$ (0.2 equiv), and $Cu(OAc)_2{\cdot}H_2O$ (0.8 mmol) in *t*-AmOH (2 mL) was stirred in sealed tubes at 120 °C. A portion of the crude solution (0.2 mL) was taken out every 15 min, purified by column chromatography, and then subjected to ^{1}H NMR measurement.

■ ASSOCIATED CONTENT

Supporting Information

Copies of NMR spectra of all new compounds and substrates **5**, X-ray single-crystal analysis, and the kinetic isotope effect experiment. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interests.

■ ACKNOWLEDGMENTS

This work was supported by grants of the Chinese National Sciences Foundation (81125021, 81373277), National Science & Technology Major Project on "Key New Drug Creation and Manufacturing Program", China (Numbers: 2012ZX09103-101-035, 2012ZX09301001-001). Supporting grants from the "Interdisciplinary Cooperation Team" Program for Science and Technology Innovation (CAS) and a grant from the State Key Laboratory of Drug Research (SIMM1302KF-08), Shanghai Institute of Materia Medica, were also appreciated.

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