JOC The Journal of Organic Chemistry

pubs.acs.org/joc Article

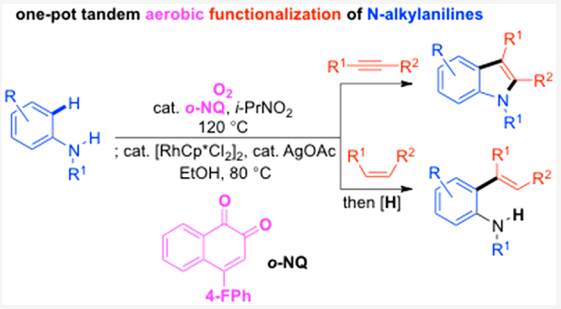
One-Pot Tandem *ortho*-Naphthoquinone-Catalyzed Aerobic Nitrosation of *N*-Alkylanilines and Rh(III)-Catalyzed C−H Functionalization Sequence to Indole and Aniline Derivatives

Tengda Si, Hun Young Kim,* and Kyungsoo Oh*

Cite This: https://dx.doi.org/10.1021/acs.joc.0c02776 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: The nitroso group served as a traceless directing group for the C−H functionalization of *N*-alkylanilines, ultimately removed after functioning either as an internal oxidant or under subsequent reducing conditions. The unique ability of *o*-NQ catalysts to aerobically oxidize the *N*-alkylanilines without using solvents and stoichiometric amounts of oxidants has rendered the new opportunity to develop the telescoped catalyst systems without a need for directly handling the hazardous *N*-nitroso compounds.



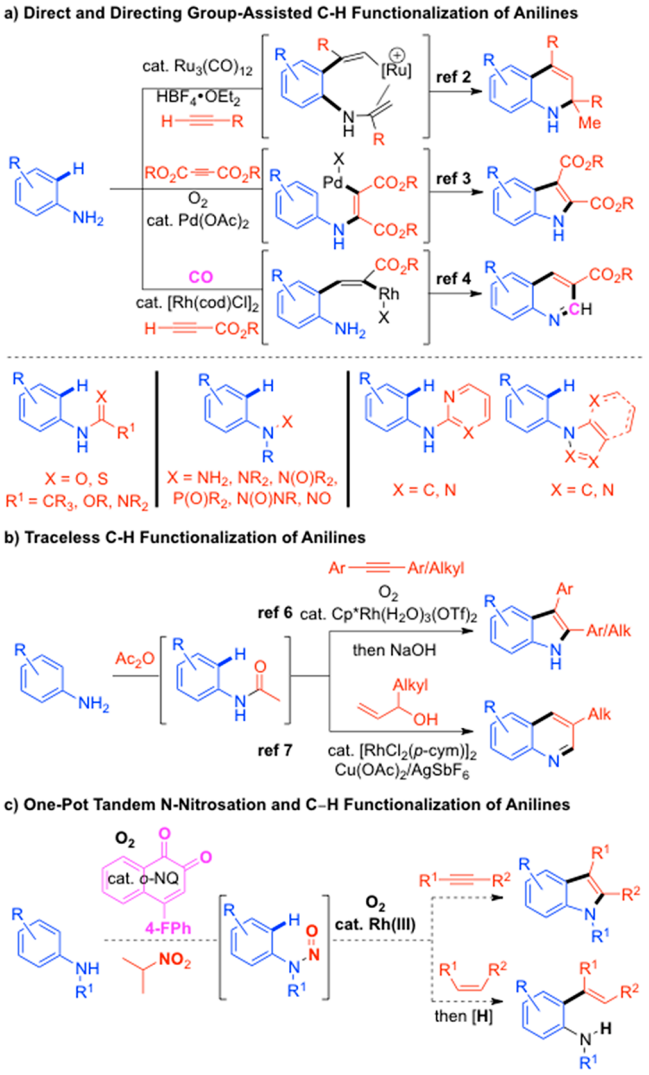
INTRODUCTION

Aniline derivatives serve as synthetic precursors to various commodity chemicals, and the strategic functionalization of anilines has been the focus of academic as well as industrial research efforts.[1] While the *ortho*-C−H activation strategies of anilines without directing groups have been explored in the Ru-catalyzed cyclization to 1,2-dihydroquinolines,[2] the Pd-catalyzed synthesis of indoles,[3] and the Rh-catalyzed synthesis of quinolines,[4] the alkyne partners in the indole synthesis are limited to highly electrophilic alkynes such as methyl acetylenedicarboxylates and methyl propiolate (Scheme 1a). Currently there are three distinctive *ortho*-C−H directing group approaches for anilines:[5] (1) the introduction of carbonyl directing groups, (2) the transformation to other functional groups, and (3) the conversion to heterocyclic directing groups. Among the directing group-assisted *ortho*-C−H functionalization strategies of anilines, the in situ acetylation of anilines allows the concomitant directing group introduction and removal in a one-pot fashion. Thus, the Huang group in 2014 demonstrated the in situ formation of acetanilides of anilines followed by the Rh-catalyzed oxidative annulation to indole derivatives after hydrolysis using NaOH (Scheme 1b).[6] In 2017, the Kapur group also disclosed the in situ acetylation of anilines followed by the Ru-catalyzed annulation to quinolines, in which the aromatization of acetanilide products concomitantly removed the directing group.[7] While the one-pot introduction of directing group and removal has opened new opportunities for the traceless C−H functionalizations,[8] the majority of directing group strategies requires the prefunctionalization of anilines. In particular, the recent emergence of *N*-nitroso directing groups has spurred the rapid advancement of C−H functionalization of anilines.[9] Nevertheless, the preparation of *N*-nitroso compounds with the use of stoichiometric amounts of oxidants[10] combined with the inherent toxicity associated with *N*-nitroso compounds[11] calls for new catalytic approaches to the *N*-nitrosation as well as one-pot/tandem C−H functionalization of *N*-nitroso compounds. Recently, our group developed the *ortho*-naphthoquinone (***o*-NQ**)-catalyzed aerobic *N*-nitrosation of amines, where 2-nitropropane served as the source of "NO" and molecular oxygen as the sole oxidant.[12] Encouraged by the mild reaction conditions of the ***o*-NQ**-catalyzed aerobic *N*-nitrosation of amines without needs for solvent combined with the synthetic versatility of *N*-nitrosoaniline derivatives as a directing group,[9] we envisioned the one-pot *N*-nitrosation followed by the C−H functionalization of in situ generated *N*-nitrosoanilines (Scheme 1c). Herein, we report the aerobic C−H functionalization of anilines with alkynes and alkenes via *N*-nitrosoaniline intermediates to give the highly substituted indole and aniline derivatives. The successful implementation of one-pot *N*-nitrosation, C−H functionalization, and removal of the nitroso group owes to the fact that the involved catalyst systems are tolerant to moisture and air, the key features for the development of practical catalytic transformations.

Received: November 19, 2020

https://dx.doi.org/10.1021/acs.joc.0c02776
J. Org. Chem. XXXX, XXX, XXX−XXX

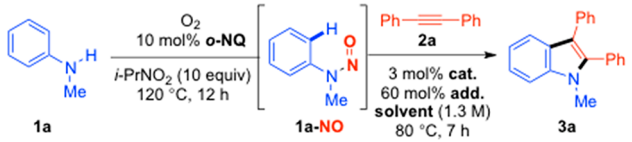
Scheme 1. C−H Functionalization Strategies for Anilines



RESULTS AND DISCUSSION

The development of one-pot *N*-nitrosation of anilines and the C−H activation sequence heavily relies on the efficiency as well as the effectiveness of the ***o*-NQ**-catalyzed aerobic *N*-nitrosation of anilines. Thus, the previous aerobic *N*-nitrosation conditions for secondary/tertiary amines were further optimized for *N*-methylaniline **1a**: 10 mol % of ***o*-NQ** catalyst and 10 equiv of *i*-$PrNO_2$ as the "NO" source at 120 °C for 12 h.[13] Thus, after the *N*-methylaniline **1a** was subjected under the aerobic *N*-nitrosation conditions, the direct addition of alkyne **2a**, metal catalyst, and additive was tested in alcoholic solvents (Table 1). The use of commercially available $[RhCp^*Cl_2]_2$ catalyst in combination with AgOAc additive in MeOH provided the desired indole derivative **3a** in 78% yield (entry 1). The use of other silver salts such as $AgSbF_6$ lowered the isolated yield of **3a** to 42% (entry 2), possibly due to the short lifetime of $AgSbF_6$ in alcoholic solvents. Switching silver to copper additive improved the isolated yield of **3a** to 86% (entry 3). The redox function of the additives was confirmed using NaOAc, where the desired product **3a** was merely observed (entry 4). The solvent screening indicated that the use of unpurified EtOH, a class III solvent,[14] was tolerated and the reaction proceeded in a highly concentrated manner (1.3 M), which led to the 90% yield of **3a** (entries 5−8). The use of other commercially available metal catalysts was not effective (entries 9−11). The control experiments confirmed the critical roles of both Rh catalyst and silver additive, where the reaction did not proceed in the absence of either one (entries 12 and 13). The reduced amount of AgOAc additive to 30 mol % slightly lowered the yield of **3a** to 80%, as opposed to 90% upon using 60 mol % (entries 6 and 14). The reduced amount of $[RhCp^*Cl_2]_2$ catalyst from 3 to 1 mol % significantly lowered the yield of **3a** to 38% (entry 15). Finally, the reaction was conducted under argon instead of O_2, and the reduced yield of **3a** was still observed in 66% yield, possibly due to the residual O_2 content in EtOH that still promotes the generation of active Rh(III) species from $[RhCp^*Cl_2]_2$ (entry 16).

Table 1. Optimization of One-Pot Tandem Functionalization of *N*-Methylaniline[a]



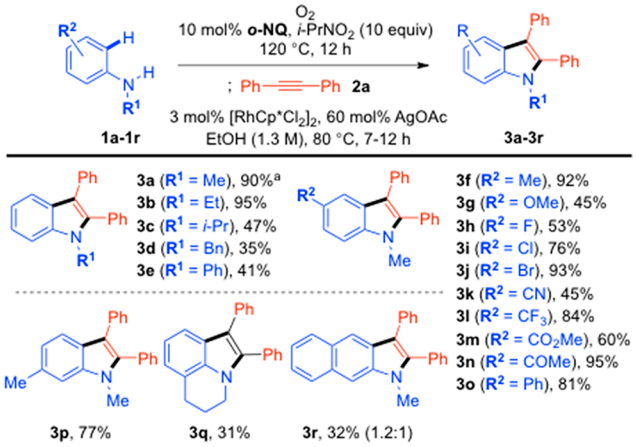
entry	catalyst	additive	solvent	yield (%)[b]
1	$[RhCp^*Cl_2]_2$	AgOAc	MeOH	78
2	$[RhCp^*Cl_2]_2$	$AgSbF_6$	MeOH	42
3	$[RhCp^*Cl_2]_2$	$Cu(OAc)_2$	MeOH	86
4	$[RhCp^*Cl_2]_2$	NaOAc	MeOH	<5
5	$[RhCp^*Cl_2]_2$	$Cu(OAc)_2$	EtOH	85
6	$[RhCp^*Cl_2]_2$	AgOAc	EtOH	90
7	$[RhCp^*Cl_2]_2$	AgOAc	*i*-PrOH	67
8	$[RhCp^*Cl_2]_2$	AgOAc	*t*-BuOH	30
9	$[IrCp^*Cl_2]_2$	AgOAc	EtOH	9
10	$Co(Cp^*)_2PF_6$	AgOAc	EtOH	0
11	$[RuCp^*Cl_2]_2$	AgOAc	EtOH	0
12	$[RhCp^*Cl_2]_2$		EtOH	<5
13		AgOAc	EtOH	0
14[c]	$[RhCp^*Cl_2]_2$	AgOAc	EtOH	80
15[d]	$[RhCp^*Cl_2]_2$	AgOAc	EtOH	38
16[e]	$[RhCp^*Cl_2]_2$	AgOAc	EtOH	66

[a]Reaction conditions: **1a** (0.4 mmol), *i*-$PrNO_2$ (4 mmol), and ***o*-NQ** (0.04 mmol; 10 mol %) under O_2 balloon at 120 °C for 12 h, then **2a** (0.2 mmol), **catalyst** (0.006 mmol; 3 mol %), and **additive** (0.12 mmol; 60 mol %) in **solvent** (0.15 mL) under O_2 balloon at 80 °C for 7 h. [b]Isolated yields of **3a** after column chromatography. [c]Use of 30 mol % of AgOAc. [d]Use of 1 mol % of $[RhCp^*Cl_2]_2$. [e]Reaction under argon.

The substrate scope for the optimized one-pot tandem reaction was investigated with aniline derivatives (Scheme 2). The examination of *N*-alkyl groups revealed that the presence of sterically demanding *i*-Pr group, oxidizable Bn group, and conjugated Ph group lowered the isolated yields of indole derivatives **3c−3e** to 35−47%. The electronic effect of the *para*-position of *N*-methylaniline derivatives was not apparent, where the electron-donating methoxy-substituted and the electron-withdrawing fluorine or nitrile-substituted *N*-methylanilines provided the low yields of indole products **3g**, **3h**, and **3k** in 45−53%. Nevertheless, the optimized one-pot tandem functionalization of anilines tolerated various halogen atoms and carbonyl groups, where the desired indole derivatives **3f**, **3i−3j**, and **3l−3o** were obtained in 60−95% yields. In addition, *meta*-substituted *N*-methylaniline provided the

https://dx.doi.org/10.1021/acs.joc.0c02776
J. Org. Chem. XXXX, XXX, XXX−XXX

Scheme 2. Aniline Substrate Scope for One-Pot Tandem Functionalization[a]

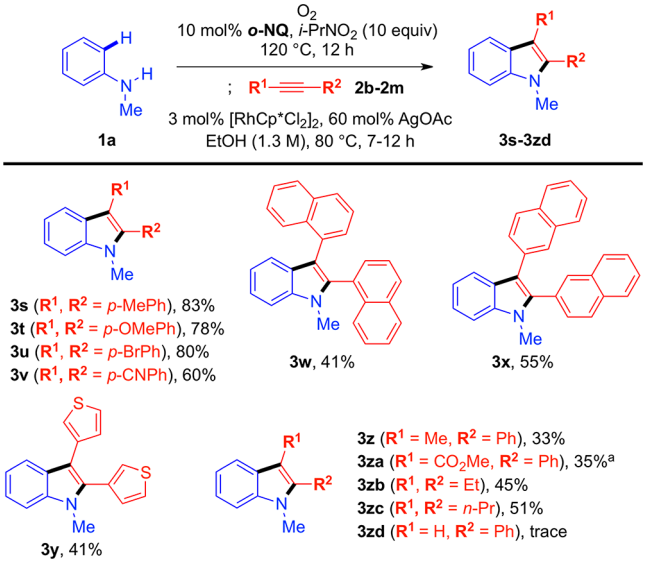


[a](a) Reaction on the 1 mmol scale in 76% yield.

regioselective formation of indole **3p** in 77% yield. However, the desired indole product **3q** from tetrahydroquinoline was obtained in 31% yield, and the use of *N*-methylnaphthalen-2-amine provided the indole product **3r** as a 1.2:1 mixture of regioisomers in 32% yield.

Next, the one-pot tandem functionalization of *N*-methylaniline **1a** was examined with a variety of alkynes (Scheme 3).

Scheme 3. Alkyne Substrate Scope for One-Pot Tandem Functionalization[a]

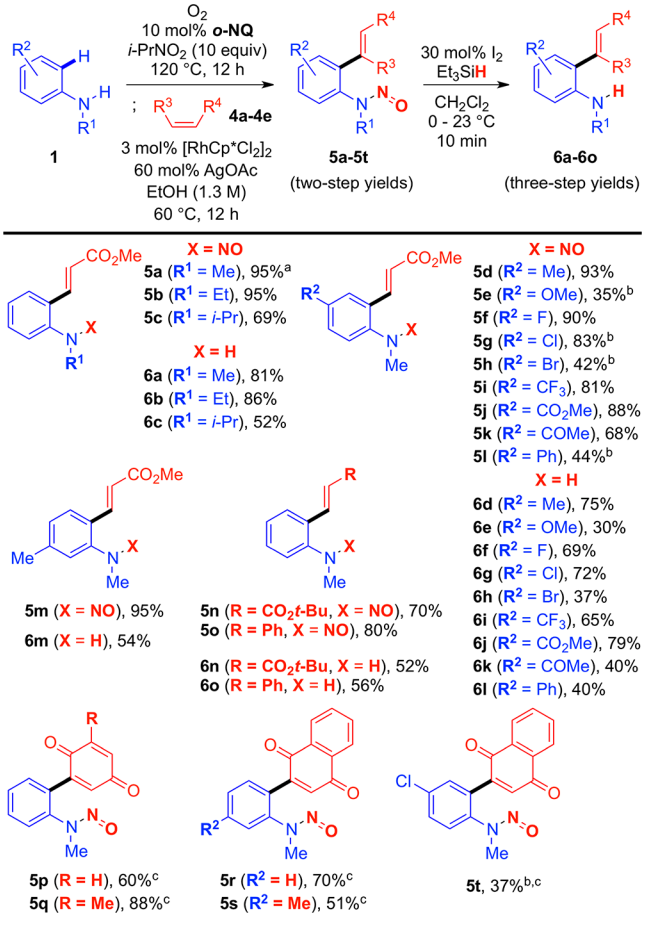


[a](a) 2.0 equiv of $Cu(OAc)_2$ was used instead of AgOAc.

The use of disubstituted alkynes with different electronic characters provided the desired indole products **3s**–**3v** in 60–83% yields. Also, the sterically demanding 1- and 2-naphthyl-substituted alkynes underwent the desired one-pot tandem reaction to give the indole product **3w**–**3x** in 41–55% yields. While the isolated yields of the indole products with thiophenyl **3y**, unsymmetric **3z**, electron-deficient **3za**, and dialkyl **3zb**–**3zc** moieties were modest, given the multiple reaction sequence of the current one-pot tandem functionalization, the rapid access to a variety of indole products without isolating the *N*-nitroso intermediates merits in terms of operational simplicity as well as enhanced environmental/safety features (no direct handling of *N*-nitroso compounds and the use of a class III solvent, unpurified EtOH, in a highly concentrated manner).

Encouraged by the facile C–H functionalization of anilines using alkynes, we further investigated the use of alkenes, instead of alkynes, under the optimized tandem reaction sequence (Scheme 4). Gratifyingly, the desired alkenylation of

Scheme 4. Alkene Substrate Scope for One-Pot Tandem Functionalization[a]



[a](a) Reaction on the1 mmol scale in 72% yield. (b) 10 mol % $AgSbF_6$ was used instead of AgOAc. (c) Reaction at 90 °C.

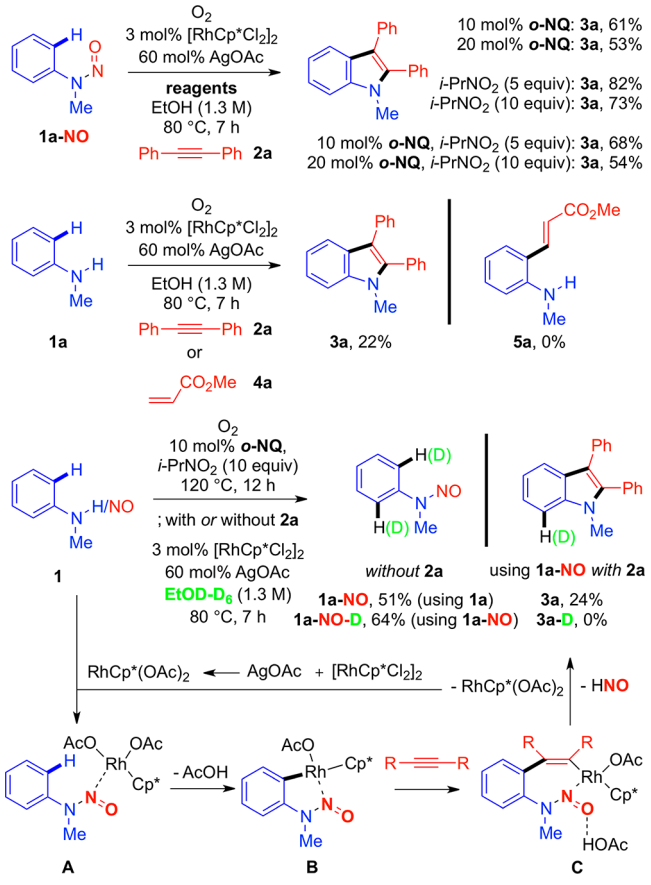
N-alkylanilines using methyl acrylate **4a** proceeded smoothly in unpurified EtOH, providing the alkenylated *N*-nitrosoanilines **5a**–**5c** in 69–95% yields. The electronic effect of *N*-methylaniline derivatives somewhat mirrored the reactions with alkynes, where the 4-methoxy-, 4-bromo-, and 4-phenyl-substituted *N*-methylanilines resulted in the products **5e**, **5h**, and **5l** in 35–44% yields. However, other functionalized *N*-methylanilines provided the corresponding alkenylated *N*-alkylanilines **5d**, **5f**–**5g**, and **5i**–**5m** in higher yields of 68–93%. The use of *t*-butyl acrylate **4b** and styrene **4c** as alkene coupling partners was also applicable, where the products **5n**–**5o** were obtained in 70–80% yields. In addition, the use of *p*-quinones also provided the desired products **5p**–**5t** at a higher reaction temperature of 90 °C in 37–88% yields. The *N*-nitro products **5** were obtained as a mixture of *anti*/*syn*-isomers due to the different orientations of R–N–N=O;[15] thus the

https://dx.doi.org/10.1021/acs.joc.0c02776
J. Org. Chem. XXXX, XXX, XXX–XXX

denitrosation of the alkenylated *N*-nitrosoanilines **5** was performed using the Kandasamy method,[16] where the I_2-catalyzed reduction of the nitroso group was performed with Et_3SiH. The application of Kandasamy's reduction protocol resulted in the formation of the alkenylated *N*-methylanilines **6** within 10 min, where the three-step reaction sequence provided the final products **6a**−**6o** in 30−86% yields from *N*-methylanilines **1**. In practice, Kandasamy's denitrosation conditions resulted in low yields of **6** upon using the crude mixture of alkenylated *N*-nitrosoanilines **5**; thus the quick removal of impurities was needed for the high yielding denitrosation conditions to give the alkenylated *N*-methylanilines **6**. Unfortunately, the *p*-quinone moiety in **5p**−**5t** was not compatible and led to the decomposition with Kandasamy's denitrosation conditions.[17]

The development of the tandem C−H functionalization of anilines benefits from the compatibility of ***o*-NQ** catalyst and 2-nitropropane in the subsequent Rh(III)-catalyzed C−H functionalization of *N*-nitrosoanilines. However, the control experiments using the *N*-nitrosoaniline **1a-NO** confirmed the deleterious effects of ***o*-NQ** catalyst and 2-nitropropane on the formation of the indole **3a** (Scheme 5). The investigation into

Scheme 5. Control Experiments for the Effect of Reagents, Nitroso Directing Group, and C−H Activation Pathway



the fate of ***o*-NQ** catalyst and 2-nitropropane after the aerobic oxidation of *N*-methylaniline **1a** suggested that the crude mixture did not contain the ***o*-NQ** catalyst,[18] and less than 3−4 equiv of 2-nitropropane was left in the crude reaction mixture.[19] Thus, it is conceivable that the residual amounts of ***o*-NQ** catalyst and 2-nitropropane are low enough in the subsequent C−H functionalization of *N*-nitrosoaniline **1a-NO**. The removal of the *N*-nitroso directing group significantly hindered the direct C−H functionalization of anilines, and this leads to the formation of **3a** in 22% yield, but not **5a**. While more studies are needed for the underlying mechanism for the direct C−H functionalization of aniline, it is possible to speculate the Rh-catalyzed hydroamination pathway[4] between *N*-methyl aniline **1a** and diphenylacetylene **2a** to give the enamine intermediate for a subsequent cyclization to give the indole product **3a**.[3] One of the key features of the current tandem C−H functionalization of anilines is the use of a class III solvent, unpurified EtOH, as opposed to other class I solvents, DCM,[9e] HFIP,[9c] and DCE,[9b−f] and class II solvents, MeOH[9a−e] and CH_3CN.[9d] Thus, the investigation into the amount of EtOH usage revealed that the reaction concentration was not critical for the efficiency of the reaction, and the optimal concentration of EtOH turned out to be 1.3 M.[20] Finally, the tandem C−H functionalization reaction in EtOD-d_6 resulted in the formation of **1a-NO** without the deuterium incorporation due to the water byproduct from the ***o*-NQ**-catalyzed aerobic *N*-nitrosation conditions. Thus, the deuterium incorporation experiment with an isolated **1a-NO** confirmed the ready C−H activation of *N*-nitrosoaniline **1a-NO** under the optimized reaction conditions, and this suggests the critical role of the *N*-nitroso group for the projected C−H activation pathway. Accordingly, the *N*-nitro directing group of **1a-NO** in EtOD-d_6 promoted the formation of **3a** without the deuterium incorporation, and this supports the direct cyclization pathway of alkenylrhodium **C** from the migratory insertion of arylrhodium **B** to the indole product **3a** without the proto-demetalation step.[9d]

CONCLUSION

In summary, we have developed the one-pot aerobic C−H functionalization of anilines via a sequence of ***o*-NQ**-catalyzed *N*-nitrosation followed by the Rh(III)-catalyzed alkenylations of in situ generated *N*-nitrosoaniline derivatives to indole and alkenylated aniline derivatives. The use of a class III solvent, unpurified EtOH, in a highly concentrated condition combined with the high tolerance of moisture and air is one of the key features of the current tandem reaction sequence. In addition, the telescoping of the *N*-nitroso compounds for the subsequent reaction avoids the hazard risk associated with the handling of the harmful *N*-nitroso compounds in the laboratory and industrial settings. Given the wide synthetic versatility of the *N*-nitroso compounds in organic synthesis, the development of tandem reaction sequences involving the ***o*-NQ**-catalyzed aerobic *N*-nitrosation of amines provides ample possibility for the preparation of value-added chemicals. Our current efforts are directed to the further exploration of one-pot tandem aerobic reactions of amines via the ***o*-NQ**-catalyzed aerobic *N*-nitrosation method, and our results will be reported in due course.

EXPERIMENTAL SECTION

General Procedures for the Synthesis of Methylanilines using Different Aryl Bromides. Aryl bromides (5 mmol, 1 equiv), 40% aqueous methylamine solution (4.1 mL, 25 mmol, 5 equiv), and copper powder (0.016 g, 5 mol %) were combined in a 30 mL screwed sealed vial and placed in an oil bath. The reaction mixture was magnetically stirred and heated to 100 °C. When the reaction was completed, the reaction mixture was cooled to room temperature, and ethyl acetate was added to extract the *N*-methylanilines. The organic

https://dx.doi.org/10.1021/acs.joc.0c02776
J. Org. Chem. XXXX, XXX, XXX−XXX

layer was separated, and the aqueous layer was extracted by the ethyl acetate (3 × 10 mL). The combined extracts were dried by anhydrous sodium sulfate and then concentrated under reduced pressure and purified by silica-gel column chromatography (eluent: 90:10 hexanes/ethyl acetate) to afford the title compounds.

N-Methyl-[1,1′-biphenyl]-4-amine. Eluent: 90:10 hexanes/ethyl acetate; 170 mg, 47% yield, white amorphous solid. ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[21] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.56 (d, J = 8.4 Hz, 2H), 7.47 (d, J = 8.4 Hz, 2H), 7.41 (t, J = 7.2 Hz, 2H), 7.28−7.25 (m, 1H), 6.70 (d, J = 9.0 Hz, 2H), 3.80 (bro, 1H), 2.89 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 148.9, 141.5, 130.3, 128.8, 128.0, 126.4, 126.2, 112.8, 30.9.

N-Methylnaphthalen-2-amine. Eluent: 90:10 hexanes/ethyl acetate; 123 mg, 39% yield, brown amorphous solid. ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[22] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.69 (d, J = 7.8 Hz, 1H), 7.67−7.63 (m, 2H), 7.40−7.37 (m, 1H), 7.24−7.21 (m, 1H), 6.92 (dd, J = 8.4, 2.4 Hz, 1H), 6.86 (d, J = 1.8 Hz, 1H), 2.92 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 146.7, 135.3, 129.0, 127.8, 126.5, 126.1, 122.2, 118.1, 104.5, 31.1.

General Procedures for the Synthesis of Symmetrical Diarylalkynes. A solution of aryl halides (1.0 equiv) and trimethylsilylacetylene (0.6 equiv), $Pd(OAc)_2$ (10 mol %), Cu(Xantphos)I (10 mol %), and Cs_2CO_3 (2 equiv) in anhydrous DMF (10 mL) was heated at 60 °C for 12−24 h under argon. After the reaction was completed, DMF was removed under reduced pressure. The remaining mixture was extracted with ethyl acetate (3 × 10 mL), and the combined organic layers were dried over anhydrous Na_2SO_4 and filtered. After removal of the solvent, the residue was purified by flash column chromatography on the silica gel (eluent: 95:5 hexanes/ethyl acetate) to afford the desired products.

4,4′-(Ethyne-1,2-diyl)dibenzonitrile. Eluent: 95:5 hexanes/ethyl acetate; 220 mg, 19% yield, brown amorphous solid. ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[23] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.68−7.66 (m, 4H), 7.64−7.62 (m, 4H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): 132.4, 132.3, 127.2, 118.4, 112.6, 91.7.

1,2-Di(naphthalen-2-yl)ethyne. Eluent: 95:5 hexanes/ethyl acetate; 250 mg, 36% yield, yellow crystalline solid. ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[24] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.11 (s, 2H), 7.86−7.83 (m, 6H), 7.64 (d, J = 8.4 Hz, 2H), 7.54−7.49 (m, 4H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 133.2, 133.0, 131.7, 128.6, 128.2, 128.0, 127.9, 126.9, 126.7, 120.7, 90.3.

1,2-Di(naphthalen-1-yl)ethyne. Eluent: 95:5 hexanes/ethyl acetate; 83 mg, 30% yield, yellow crystalline solid. ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[24] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.58 (d, J = 7.8 Hz, 2H), 7.92−7.88 (m, 6H), 7.65 (t, J = 7.8 Hz, 2H), 7.59−7.56 (m, 2H), 7.52 (t, J = 7.8 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 133.4, 130.7, 129.0, 128.5, 127.1, 126.6, 126.5, 125.5, 121.2, 92.6.

1,2-Di(thiophen-3-yl)ethyne. Eluent: 95:5 hexanes/ethyl acetate; 210 mg, 44% yield, brown amorphous solid. ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[25] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.50 (d, J = 2.4 Hz, 2H), 7.31−7.29 (m, 2H), 7.19−7.18 (m, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 130.0, 128.6, 125.5, 122.3, 84.1.

General Procedure A: Synthesis of Indole Derivatives. A flame-dried 10 mL vial was charged with *N*-alkyl aniline derivatives (0.4 mmol, 2 equiv), catalyst ***o*-NQ** (0.04 mmol, 20 mol %), and 2-nitropropane (4 mmol, 20 equiv). The solution was stirred under O_2 at 120 °C. After the reaction was complete by TLC (12 h), the reaction mixture was then cooled to room temperature. $[RhCp^*Cl_2]_2$ (0.006 mmol, 3 mol %), AgOAc (0.12 mmol, 60 mol %), and alkyne (0.2 mmol, 1 equiv) in ethanol (0.15 mL) were added to the vial. The mixture was stirred at 80 °C under O_2 for 7 h. Upon the complete consumption of alkyne, the reaction was cooled to room temperature. Volatile solvent and reagents were removed by rotary evaporation, and the residue was purified by silica gel flash chromatography using hexane/EtOAc (80:1 to 30:1) to afford the indole derivatives.

*1-Methyl-2,3-diphenyl-1H-indole (**3a**).* Eluent: 80:1 hexanes/ethyl acetate; 51 mg, 90% yield, yellow amorphous solid. The product was prepared via the general procedure A. ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9e] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.84 (d, J = 7.8 Hz, 1H), 7.45 (d, J = 8.4 Hz, 1H), 7.42−7.39 (m, 3H), 7.37−7.32 (m, 5H), 7.31 (t, J = 8.4 Hz, 2H), 7.24−7.19 (m, 2H), 3.71 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 137.6, 137.5, 135.4, 132.0, 131.3, 130.0, 128.5, 128.3, 128.2, 127.1, 125.6, 122.3, 120.3, 119.7, 115.2, 109.7, 31.1.

For the scale-up reaction, a flame-dried 25 mL flask was charged with *N*-alkyl aniline derivatives (2.0 mmol), catalyst ***o*-NQ** (0.20 mmol, 10 mol %), and 2-nitropropane (20 mmol). The solution was stirred under O_2 at 120 °C. After the reaction was complete by TLC (24 h), the reaction mixture was then cooled to room temperature. $[RhCp^*Cl_2]_2$ (0.030 mmol, 3 mol %), AgOAc (0.60 mmol, 60 mol %), and diphenylacetylene (1.0 mmol) in ethanol (0.75 mL) were added to the vial. The mixture was stirred at 80 °C under O_2 for 18 h. Upon the complete consumption of alkyne, the reaction was cooled to room temperature. Volatile solvent and reagents were removed by rotary evaporation, and the residue was purified by silica gel flash chromatography using hexane/EtOAc (80:1) to afford the indole derivative **3a** in 76% yield (215 mg).

*1-Ethyl-2,3-diphenyl-1H-indole (**3b**).* Eluent: 80:1 hexanes/ethyl acetate; 56 mg, 95% yield, yellow crystalline solid. The product was prepared via the general procedure A. ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9e] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.82 (d, J = 7.2 Hz, 1H), 7.45 (d, J = 7.8 Hz, 1H), 7.41−7.37 (m, 3H), 7.36−7.34 (m, 2H), 7.32−7.28 (m, 3H), 7.28−7.24 (m, 2H), 7.21−7.15 (m, 2H), 4.15 (q, J = 7.2 Hz, 2H), 1.30 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 137.4, 136.2, 135.4, 132.4, 131.2, 129.9, 128.6, 128.2, 127.4, 125.5, 122.2, 120.2, 119.9, 115.5, 109.9, 38.8, 15.5.

*1-Isopropyl-2,3-diphenyl-1H-indole (**3c**).* Eluent: 80:1 hexanes/ethyl acetate; 29 mg, 47% yield, yellow crystalline solid. The product was prepared via the general procedure A. ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9e] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.82 (d, J = 7.8 Hz, 1H), 7.68 (d, J = 8.4 Hz, 1H), 7.42−7.39 (m, 3H), 7.35−7.32 (m, 2H), 7.30−7.24 (m, 5H), 7.20−7.15 (m, 2H), 4.59 (septet, J = 6.6 Hz, 2H), 1.65 (t, J = 6.6 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 137.7, 135.4, 134.7, 132.9, 131.3, 130.1, 128.5, 128.3, 128.2(1), 128.1(5), 125.5, 121.6, 120.0, 119.8, 115. 3, 112.4, 48.0, 21.7.

*1-Benzyl-2,3-diphenyl-1H-indole (**3d**).* Eluent: 70:1 hexanes/ethyl acetate; 25 mg, 35% yield, yellow amorphous solid. The product was prepared via the general procedure A. ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9e] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.86−7.84 (m, 1H), 7.36 (dd, J = 7.8, 1.2 Hz, 1H), 7.34−7.26 (m, 10H), 7.26−7.18 (m, 4H), 7.04 (d, J = 6.6 Hz, 2H), 5.32 (s, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 138.2, 138.0, 137.1, 135.2, 131.9, 131.2, 130.0, 128.8, 128.5, 128.3, 127.5, 127.3, 126.3, 125.7, 122.5, 120.6, 119.9, 115.8, 110.7, 47.7.

*1,2,3-Triphenyl-1H-indole (**3e**).* Eluent: 70:1 hexanes/ethyl acetate; 28 mg, 41% yield, yellow crystalline solid. The product was prepared via the general procedure A. ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9e] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.82−7.80 (m, 1H), 7.38 (t, J = 7.2 Hz, 4H), 7.36−7.31 (m, 4H), 7.26−7.22 (m, 5H), 7.18−7.12 (m, 3H), 7.11−7.08 (m, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 138.3, 138.0, 137.2, 135.1, 131.7, 131.3, 130.4, 129.2, 128.4(3), 128.4(0), 127.7, 127.5, 127.3, 126.1, 122.9, 121.0, 119.7, 117.9, 116.8, 110.8.

*1,5-Dimethyl-2,3-diphenyl-1H-indole (**3f**).* Eluent: 80:1 hexanes/ethyl acetate; 55 mg, 92% yield, yellow amorphous solid. The product was prepared via the general procedure A. ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9e] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.63 (s, 1H), 7.42−7.39 (m, 3H), 7.38−7.30 (m, 7H), 7.23−7.20 (m, 1H), 7.18 (dd, J =

https://dx.doi.org/10.1021/acs.joc.0c02776
J. Org. Chem. XXXX, XXX, XXX−XXX

8.4, 1.2 Hz, 1H), 3.69 (s, 3H), 2.52 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 137.9, 135.9, 135.4, 132.2, 131.3, 130.0, 129.6, 128.5, 128.3, 128.1, 127.3, 125.5, 123.9, 119.3, 114.8, 109.4, 31.1, 21.7.

*5-Methoxy-1-methyl-2,3-diphenyl-1H-indole (**3g**).* Eluent: 60:1 hexanes/ethyl acetate; 28 mg, 45% yield, yellow amorphous solid. The product was prepared via the general procedure A. ^1H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9e] ^1H NMR ($CDCl_3$, 600 MHz): δ 7.40−7.35 (m, 3H), 7.33−7.30 (m, 3H), 7.29 (dd, J = 7.2, 1.8 Hz, 3H), 7.25 (d, J = 1.8 Hz, 1H), 7.20−7.17 (m, 1H), 3.86 (s, 3H), 3.66 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 154.9, 138.5, 135.5, 132.1, 132.0, 131.2, 129.9, 128.5, 128.4, 128.1, 127.4, 125.6, 115.0, 112.6, 110.5, 101.4, 56.2, 31.2.

*5-Fluoro-1-methyl-2,3-diphenyl-1H-indole (**3h**).* Eluent: 70:1 hexanes/ethyl acetate; 32 mg, 53% yield, yellow amorphous solid. The product was prepared via the general procedure A. ^1H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9e] ^1H NMR ($CDCl_3$, 600 MHz): δ 7.46 (dd, J = 9.0, 2.4 Hz, 1H), 7.41−7.39 (m, 3H), 7.35−7.31 (m, 3H), 7.30−7.26 (m, 4H), 7.21−7.17 (m, 1H), 7.06 (dt, J = 9.0, 2.4 Hz, 1H), 3.68 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 158.7 (C−F, $^1J_{C-F}$ = 232.7 Hz), 139.4, 134.9, 134.1, 131.7, 131.2, 129.8, 128.6, 128.4(3), 128.3(8), 127.4 (C−F, $^3J_{C-F}$ = 10.1 Hz), 125.8, 115.3 (C−F, $^3J_{C-F}$ = 4.4 Hz), 110.6 (C−F, $^2J_{C-F}$ = 25.8 Hz), 110.4 (C−F, $^3J_{C-F}$ = 10.1 Hz), 104.6 (C−F, $^2J_{C-F}$ = 23.0 Hz), 31.3. ^{19}F NMR ($CDCl_3$, 564 MHz): δ −124.0.

*5-Chloro-1-methyl-2,3-diphenyl-1H-indole (**3i**).* Eluent: 70:1 hexanes/ethyl acetate; 48 mg, 76% yield, yellow amorphous solid. The product was prepared via the general procedure A. ^1H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9f] ^1H NMR ($CDCl_3$, 600 MHz): δ 7.78 (d, J = 1.8 Hz, 1H), 7.42−7.39 (m, 3H), 7.35−7.31 (m, 3H), 7.31−7.25 (m, 5H), 7.23−7.20 (m, 1H), 3.68 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 139.1, 135.9, 134.7, 131.5, 131.2, 129.9, 128.6, 128.4(4), 128.4(2), 128.1, 126.1, 126.0, 122.5, 119.1, 115.0, 110.8, 31.2.

*5-Bromo-1-methyl-2,3-diphenyl-1H-indole (**3j**).* Eluent: 70:1 hexanes/ethyl acetate; 67 mg, 93% yield, yellow amorphous solid. The product was prepared via the general procedure A. ^1H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9f] ^1H NMR ($CDCl_3$, 600 MHz): δ 7.92 (d, J = 1.2 Hz, 1H), 7.42−7.38 (m, 4H), 7.35−7.32 (m, 2H), 7.32−7.27 (m, 5H), 7.23−7.19 (m, 1H), 3.67 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 138.9, 136.1, 134.6, 131.2, 129.9, 128.8, 128.6, 128.5, 126.0, 125.0, 122.2, 114.9, 113.6, 111.2, 31.2.

*1-Methyl-2,3-diphenyl-1H-indole-5-carbonitrile (**3k**).* Eluent: 30:1 hexanes/ethyl acetate; 28 mg, 45% yield, yellow amorphous solid. The product was prepared via the general procedure A. ^1H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9f] ^1H NMR ($CDCl_3$, 600 MHz): δ 8.11 (d, J = 1.2 Hz, 1H), 7.52 (dd, J = 8.4, 1.2 Hz, 1H), 7.45 (d, J = 7.8 Hz, 1H), 7.43−7.40 (m, 3H), 7.34−7.29 (m, 4H), 7.26−7.22 (m, 3H), 3.71 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 139.9, 138.9, 133.8, 131.1, 130.9, 129.9, 128.8(8), 128.7(8), 128.6, 127.1, 126.5, 125.5, 125.1, 121.0, 116.1, 110.5, 103.3, 31.4.

*1-Methyl-2,3-diphenyl-5-(trifluoromethyl)-1H-indole (**3l**).* Eluent: 70:1 hexanes/ethyl acetate; 59 mg, 84% yield, yellow amorphous solid. The product was prepared via the general procedure A. ^1H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9f] ^1H NMR ($CDCl_3$, 600 MHz): δ 8.07 (s, 1H), 7.54 (dd, J = 6.4, 1.8 Hz, 1H), 7.48 (d, J = 9.0 Hz, 1H), 7.43−7.40 (m, 3H), 7.36−7.28 (m, 6H), 7.25−7.22 (s, 1H), 3.73 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 139.5, 138.7, 134.4, 131.3, 131.2, 130.0, 128.7, 128.6(1), 128.5(8), 126.6, 126.2, 125.6 (C−F, $^1J_{C-F}$ = 225 Hz), 122.7 (C−F, $^2J_{C-F}$ = 26.4 Hz), 119.0 (C−F, $^3J_{C-F}$ = 3.6 Hz), 117.5 (C−F, $^3J_{C-F}$ = 1.9 Hz), 116.2, 110.0, 31.3. ^{19}F NMR ($CDCl_3$, 564 MHz): δ −60.0.

*Methyl 1-Methyl-2,3-diphenyl-1H-indole-5-carboxylate (**3m**).* Eluent: 40:1 hexanes/ethyl acetate; 41 mg, 60% yield, yellow amorphous solid. The product was prepared via the general procedure A. ^1H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9e] ^1H NMR ($CDCl_3$, 600 MHz): δ 8.53 (d, J = 1.2 Hz, 1H), 8.02 (dd, J = 9.0, 1.8 Hz, 1H), 7.42 (d, J = 8.4 Hz, 1H), 7.40 (dd, J = 8.4, 1.8 Hz, 3H), 7.35−7.32 (m, 2H), 7.31 (J = 4.2 Hz, 4H), 7.34−7.20 (m, 1H), 3.93 (s, 3H), 3.70 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 168.3, 139.8, 139.1, 134.5, 131.4, 131.2, 130.1, 128.6, 128.5, 126.8, 126.1, 123.7, 122.8, 122.3, 116.6, 109.4, 52.0, 31.3.

*1-(1-Methyl-2,3-diphenyl-1H-indol-5-yl)ethan-1-one (**3n**).* Eluent: 50:1 hexanes/ethyl acetate; 62 mg, 95% yield, yellow amorphous solid. The product was prepared via the general procedure A. ^1H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9e] ^1H NMR ($CDCl_3$, 600 MHz): δ 8.43 (d, J = 1.8 Hz, 1H), 7.99 (dd, J = 9.0, 1.2 Hz, 1H), 7.44 (d, J = 9.0 Hz, 1H), 7.42−7.40 (m, 3H), 7.35−7.30 (m, 6H), 7.25−7.22 (m, 1H), 3.71 (s, 3H), 2.67 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 198.4, 139.7, 139.3, 134.4, 131.3, 131.2, 130.4, 130.0, 128.6, 128.5, 126.7, 126.2, 122.6, 122.0, 116.9, 109.6, 31.3, 26.8.

*1-Methyl-2,3,5-triphenyl-1H-indole (**3o**).* Eluent: 50:1 hexanes/ethyl acetate; 58 mg, 81% yield, orange amorphous solid. The product was prepared via the general procedure A. ^1H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9f] ^1H NMR ($CDCl_3$, 600 MHz): δ 8.07 (d, J = 1.8 Hz, 1H), 7.72 (d, J = 7.8 Hz, 2H), 7.62 (dd, J = 9.0, 1.8 Hz, 1H), 7.52 (d, J = 8.4 Hz, 1H), 7.49 (t, J = 7.8 Hz, 2H), 7.46−7.42 (m, 3H), 7.41−7.38 (m, 4H), 7.38−7.33 (m, 3H), 7.26−7.23 (m, 1H), 3.75 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 142.8, 138.5, 137.0, 135.2, 134.0, 131.9, 131.2, 130.1, 128.6, 128.5, 128.4, 128.2, 127.6, 126.5, 125.8, 122.2, 118.3, 115.7, 110.0, 31.2.

*1,6-Dimethyl-2,3-diphenyl-1H-indole (**3p**).* Eluent: 80:1 hexanes/ethyl acetate; 46 mg, 77% yield, yellow amorphous solid. The product was prepared via the general procedure A. ^1H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9f] ^1H NMR ($CDCl_3$, 600 MHz): δ 7.68 (d, J = 8.4 Hz, 1H), 7.40−7.35 (m, 3H), 7.33−7.29 (m, 4H), 7.28−7.24 (m, 2H), 7.21 (s, 1H), 7.18−7.15 (m, 1H), 7.03 (d, J = 7.8 Hz, 1H), 3.64 (s, 3H), 2.55 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 137.9, 137.2, 135.6, 132.2(2), 132.2(0), 131.3, 129.9, 128.5, 128.3, 128.0, 125.5, 125.0, 122.0, 119.4, 115.1, 109.7, 31.0, 22.1.

*1,2-Diphenyl-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinoline (**3q**).* Eluent: 50:1 hexanes/ethyl acetate; 19 mg, 31% yield, yellow crystalline solid. The product was prepared via the general procedure A. ^1H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9e] ^1H NMR ($CDCl_3$, 600 MHz): δ 7.64 (d, J = 7.8 Hz, 1H), 7.41−7.35 (m, 7H), 7.29 (t, J = 7.8 Hz, 2H), 7.20−7.17 (m, 1H), 7.11 (t, J = 7.8 Hz, 1H), 7.01 (d, J = 1.2 Hz, 1H), 4.10 (t, J = 6.0 Hz, 2H), 3.07 (t, J = 6.0 Hz, 2H), 2.25 (qui, J = 6.0 Hz, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 136.2, 135.8, 134.5, 132.0, 130.9, 129.8, 128.5, 128.3, 128.0, 125.5, 125.1, 122.2, 120.4, 119.3, 117.2, 114.6, 43.3, 25.3, 23.1.

*1-Methyl-2,3-diphenyl-1H-benzo[f]indole (**3r**).* Eluent: 50:1 hexanes/ethyl acetate; 21 mg, 32% yield (1.2:1), yellow amorphous solid, mp 139−142 °C. The product was prepared via the general procedure A. ^1H NMR ($CDCl_3$, 600 MHz): δ 8.29 (s, 1.00H), 7.99 (d, J = 7.8 Hz, 1.20H), 7.96 (d, J = 8.4 Hz, 1.11H), 7.91 (d, J = 7.8 Hz, 0.92H), 7.85 (d, J = 8.4 Hz, 0.96H), 7.80 (s, 1.00H), 7.70 (d, J = 9.0 Hz, 0.82H), 7.61 (d, J = 8.4 Hz, 0.91H), 7.43−7.39 (m, 10.66H), 7.37−7.29 (m, 9.80H), 7.28−7.26 (m, 2.34H), 7.25−7.22 (m, 1.37H), 3.82 (s, 2.74H), 3.77 (s, 3.26H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 141.6, 138.5, 137.2, 137.0, 135.2, 133.6, 131.9, 131.8, 131.7, 131.3, 131.2, 130.6, 130.1, 130.0, 129.3, 129.0, 128.8(4), 128.7(6), 128.6, 128.5, 128.3, 128.2(7), 128.1(5), 127.7, 127.6, 126.7, 125.8, 125.4, 124.0, 123.5, 123.4, 123.1, 122.7, 120.5, 118.2, 117.2, 111.3, 104.9, 31.5, 31.4. IR (neat): 1600, 1459, 1442, 1402, 1362, 1273, 1068, 1027, 844, 799, 781, 714, 697 cm^{-1}. HRMS (ESI): m/z calcd for $C_{25}H_{19}N$ $[M + H]^+$, 334.1590; found, 334.1599.

*1-Methyl-2,3-di-p-tolyl-1H-indole (**3s**).* Eluent: 80:1 hexanes/ethyl acetate; 51 mg, 83% yield, yellow crystalline solid. The product was prepared via the general procedure A. ^1H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature

https://dx.doi.org/10.1021/acs.joc.0c02776
J. Org. Chem. XXXX, XXX, XXX−XXX

data.[9e] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.83 (d, J = 8.4 Hz, 1H), 7.44 (d, J = 8.4 Hz, 1H), 7.34 (t, J = 7.2 Hz, 1H), 7.28−7.21 (m, 7H), 7.14 (d, J = 7.2 Hz, 2H), 3.71 (s, 3H), 2.44 (s, 3H), 2.38 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 137.9, 137.8, 137.4, 135.0, 132.5, 131.1, 129.8, 129.2, 129.1(3), 129.0(5), 127.2, 122.1, 120.1, 119.7, 114.9, 109.6, 31.0, 21.5, 21.3.

*2,3-Bis(4-methoxyphenyl)-1-methyl-1H-indole (**3t**).* Eluent: 70:1 hexanes/ethyl acetate; 53 mg, 78% yield, yellow amorphous solid. The product was prepared via the general procedure A. ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9e] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.78 (d, J = 7.8 Hz, 1H), 7.41 (d, J = 8.4 Hz, 1H), 7.31 (t, J = 7.2 Hz, 1H), 7.30 (td, J = 7.8, 1.2 Hz, 1H), 7.28−7.24 (m, 3H), 7.19 (t, J = 8.4 Hz, 1H), 6.94−6.92 (m, 2H), 6.87−6.85 (m, 2H), 3.85 (s, 3H), 3.81 (s, 3H), 3.67 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 159.4, 157.6, 137.3, 137.3, 132.4, 130.9, 127.9, 127.2, 124.3, 122.0, 120.1, 119.6, 114.5, 114.0, 113.8, 109.6, 55.4, 55.3, 31.0.

*2,3-Bis(4-bromophenyl)-1-methyl-1H-indole (**3u**).* Eluent: 80:1 hexanes/ethyl acetate; 70 mg, 80% yield, yellow crystalline solid. The product was prepared via the general procedure A. ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9e] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.74 (d, J = 8.4 Hz, 1H), 7.55 (dd, J = 6.0, 1.8 Hz, 2H), 7.44−7.41 (m, 3H), 7.34 (td, J = 8.4, 1.8 Hz, 1H), 7.30−7.20 (m, 1H), 7.19 (dd, J = 6.0, 1.8 Hz, 2H), 7.16 (dd, J = 8.4, 1.8 Hz, 2H), 3.68 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 137.6, 136.6, 134.0, 132.7, 132.0, 131.6, 131.5, 130.6, 126.7, 122.8, 120.7, 119.8, 119.5, 114.5, 109.9, 31.1.

*4,4′-(1-Methyl-1H-indole-2,3-diyl)dibenzonitrile (**3v**).* Eluent: 30:1 hexanes/ethyl acetate; 40 mg, 60% yield, yellow amorphous solid, mp 265−267 °C. The product was prepared via the general procedure A. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.74 (d, J = 8.4 Hz, 1H), 7.72 (dd, J = 6.6, 1.8 Hz, 2H), 7.57 (dd, J = 6.6, 1.2 Hz, 2H), 7.47 (d, J = 8.4 Hz, 1H), 7.44 (dd, J = 6.6, 1.8 Hz, 2H), 7.39 (t, J = 7.2 Hz, 1H), 7.34 (dd, J = 6.6, 2.4 Hz, 2H), 7.26 (t, J = 8.4 Hz, 1H), 3.72 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 139.8, 138.0, 136.4, 136.1, 132.6, 132.4, 131.8, 130.3, 126.4, 123.7, 121.5, 119.5, 119.2, 118.4, 115.0, 112.5, 110.3, 109.5, 31.4. IR (neat): 2229, 1605, 1469, 1370, 1264, 1090, 1017, 869, 833, 751 cm^{-1}. HRMS (ESI): m/z calcd for $C_{23}H_{15}N_3$ $[M + H]^+$, 334.1338; found, 334.1347.

*1-Methyl-2,3-di(naphthalen-1-yl)-1H-indole (**3w**).* Eluent: 50:1 hexanes/ethyl acetate; 31 mg, 41% yield, yellow amorphous solid, mp 195−198 °C. The product was prepared via the general procedure A. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.04 (d, J = 8.4 Hz, 1.0H), 7.91−7.89 (m, 0.91H), 7.86 (t, J = 8.4 Hz, 1.57H), 7.81−7.75 (m, 3.34H), 7.73 (d, J = 8.4 Hz, 1H), 7.69−7.64 (m, 2.53H), 7.55−7.51 (m, 4.96H), 7.49−7.46 (m, 2H), 7.43−7.39 (m, 1.53H), 7.38−7.29 (m, 4.94H), 7.25−7.19 (m, 2.84H), 7.17−7.09 (m, 3.49H), 7.00 (d, J = 6.0 Hz, 1.0H), 3.57 (s, 2.07H), 3.53 (s, 2.85H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 137.9, 137.3, 137.2, 137.1, 133.8, 133.7, 133.5, 133.4, 133.1, 132.9(3), 132.9(0), 132.8, 130.0, 129.8, 129.0, 128.6, 128.5, 128.3, 128.2, 128.0, 127.3, 127.0(3), 127.0(0), 126.9(5), 126.9(1), 126.1, 126.0(4), 125.9(6), 125.7, 125.5, 125.3, 125.2, 125.0, 122.2, 122.1, 120.8, 120.5, 120.0(3), 119.9(5), 115.4, 115.2, 109.6, 31.1. IR (neat): 1595, 1469, 1359, 1265, 1247, 1014, 803, 777, 751, 702 cm^{-1}. HRMS (ESI): m/z calcd for $C_{29}H_{21}N$ $[M + H]^+$, 384.1746; found, 384.1756.

*1-Methyl-2,3-di(naphthalen-2-yl)-1H-indole (**3x**).* Eluent: 50:1 hexanes/ethyl acetate; 42 mg, 55% yield, yellow amorphous solid, mp 181−183 °C. The product was prepared via the general procedure A. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.98 (s, 1H), 7.96 (d, J = 7.2 Hz, 1H), 7.90 (s, 1H), 7.88 (d, J = 7.8 Hz, 1H), 7.82 (t, J = 7.2 Hz, 2H), 7.70 (t, J = 9.0 Hz, 2H), 7.65 (d, J = 7.8 Hz, 1H), 7.55−7.49 (m, 3H), 7.46 (dd, J = 8.4, 1.2 Hz, 1H), 7.45−7.41 (m, 2H), 7.39 (t, J = 7.8 Hz, 1H), 7.35 (dd, J = 8.4, 1.2 Hz, 1H), 7.29 (t, J = 7.8 Hz, 1H), 3.78 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 138.1, 137.8, 133.8, 133.3, 133.0, 132.9, 131.9, 130.5, 129.5, 128.9, 128.8, 128.3, 128.2(0),128.1(7), 127.9(1), 127.8(8), 127.7(3), 127.7(0), 127.3, 126.7, 126.5, 125.9, 125.3, 122.5, 120.6, 119.8, 115.5, 109.9, 31.3. IR (neat): 1629, 1601, 1547, 1470, 1402, 1373, 1336, 1313, 1265, 1241, 1087, 1019, 863, 826, 740 cm^{-1}. HRMS (ESI): m/z calcd for $C_{29}H_{21}N$ $[M + H]^+$, 384.1746; found, 384.1755.

*1-Methyl-2,3-di(thiophen-3-yl)-1H-indole (**3y**).* Eluent: 40:1 hexanes/ethyl acetate; 24 mg, 41% yield, yellow amorphous solid, mp 99−101 °C. The product was prepared via the general procedure A. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.82 (d, J = 7.8 Hz, 1H), 7.41−7.39 (m, 1H), 7.38 (d, J = 8.4 Hz, 1H), 7.32−7.28 (m, 2H), 7.25 (t, J = 8.4 Hz, 1H), 7.20 (t, J = 7.8 Hz, 1H), 7.16 (dd, J = 8.4, 1.8 Hz, 2H), 7.07−7.06 (m, 1H), 6.96 (dd, J = 8.4, 1.8 Hz, 1H), 3.69 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 137.3, 135.4, 132.9, 132.2, 129.6, 1287, 126.9, 126.2, 125.9, 124.7, 122.4, 120.3, 119.8, 110.9, 109.6, 31.0. IR (neat): 1468, 1342, 1316, 1254, 791, 743, 671 cm^{-1}. HRMS (ESI): m/z calcd for $C_{17}H_{13}NS_2$ $[M + H]^+$, 296.0562; found, 296.0562.

*1,2-Dimethyl-3-phenyl-1H-indole (**3z**).* Eluent: 80:1 hexanes/ethyl acetate; 15 mg, 33% yield, yellow amorphous solid. The product was prepared via the general procedure A. ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[26] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.62 (d, J = 7.8 Hz, 1H), 7.50 (t, J = 8.4 Hz, 2H), 7.44−7.40 (m, 3H), 7.35 (d, J = 7.8 Hz, 1H), 7.27 (t, J = 7.8 Hz, 1H), 7.17 (t, J = 7.8 Hz, 1H), 3.63 (s, 3H), 2.30 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 137.8, 137.3, 132.3, 130.8, 128.6, 128.5, 127.9, 121.9, 119.2, 118.9, 109.4, 108.7, 31.1, 9.5.

*Methyl-1-methyl-3-phenyl-1H-indole-2-carboxylate (**3za**).* Eluent: 40:1 hexanes/ethyl acetate; 19 mg, 35% yield, yellow gum. The product was prepared via the general procedure A. ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9f] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.24 (dd, J = 7.2, 1.8 Hz, 1H), 7.53−7.49 (m, 3H), 7.43−7.39 (m, 3H), 7.36−7.32 (m, 2H), 3.76 (s, 3H), 3.58 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 165.7, 147.1, 136.9, 131.6, 130.4, 129.1, 128.2, 126.7, 123.0, 122.3, 122.1, 109.9, 105.1, 50.9, 31.0.

*2,3-Diethyl-1-methyl-1H-indole (**3zb**).* Eluent: 80:1 hexanes/ethyl acetate; 17 mg, 45% yield, yellow liquid. The product was prepared via the general procedure A. ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[26] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.55 (d, J = 7.2 Hz, 1H), 7.25 (d, J = 7.8 Hz, 1H), 7.16 (t, J = 7.8 Hz, 1H), 7.07 (t, J = 7.2 Hz, 1H), 3.68 (s, 3H), 2.78 (q, J = 7.8 Hz, 2H), 2.75 (q, J = 7.8 Hz, 2H), 1.24 (t, J = 7.8 Hz, 3H), 1.22 (t, J = 7.8 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 138.1, 136.8, 127.6, 120.6, 118.7, 118.3, 112.8, 108.7, 29.5, 17.8(1), 17.7(5), 16.4, 15.1.

*1-Methyl-2,3-dipropyl-1H-indole (**3zc**).* Eluent: 80:1 hexanes/ethyl acetate; 22 mg, 51% yield, yellow liquid. The product was prepared via the general procedure A. ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[26] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.56 (d, J = 8.4 Hz, 1H), 7.27 (d, J = 7.8 Hz, 1H), 7.16 (td, J = 7.8, 1.2 Hz, 1H), 7.10−7.07 (m, 1H), 3.68 (s, 3H), 2.74 (t, J = 7.8 Hz, 2H), 2.71 (t, J = 7.8 Hz, 2H), 1.68 (sext, J = 7.8 Hz, 2H), 1.63 (sext, J = 7.8 Hz, 2H), 1.03 (t, J = 7.8 Hz, 3H), 1.00 (t, J = 7.8 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 137.0, 136.8, 128.0, 120.5, 118.6, 118.5, 111.8, 108.7, 29.7, 26.9, 26.7, 24.6, 23.7, 14.5, 14.2.

General Procedure B: Synthesis of Alkenylated Products. A flame-dried 10 mL vial was charged with *N*-alkyl aniline derivatives (0.4 mmol, 2 equiv), catalyst ***o*-NQ** (0.04 mmol, 10 mol %), and 2-nitropropane (4 mmol, 20 equiv). The solution was stirred under O_2 at 120 °C. After the reaction was complete by TLC (12 h), the reaction mixture was cooled to room temperature. $[RhCp^*Cl_2]_2$ (0.006 mmol, 3 mol %), AgOAc (0.12 mmol, 60 mol %), and alkene (0.2 mmol, 1 equiv) in ethanol (0.15 mL) were added to the vial. The mixture was stirred at 60 °C under O_2 for 7−12 h. Upon the complete consumption of alkyne, the reaction was cooled to room temperature. Volatile solvent and reagents were removed by rotary evaporation, and the residue was purified by silica gel flash chromatography using hexane/EtOAc (50:1 to 30:1) to afford the alkenylated product.

*(E)-Methyl 3-(2-(Methyl(nitroso)amino)phenyl)acrylate (**5a**).* Eluent: 50:1 hexanes/ethyl acetate; 42 mg, 95% yield, yellow crystalline solid. The product was prepared via the general procedure B. The title compound was obtained as an inseparable mixture of *syn*- and *anti*-isomers due to the different conformations of the N═O bond (>20:1). ^{1}H NMR and ^{13}C NMR spectra for this compound are

https://dx.doi.org/10.1021/acs.joc.0c02776
J. Org. Chem. XXXX, XXX, XXX−XXX

consistent with previously reported literature data.[9a] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.74 (dd, J = 7.8, 1.8 Hz, 1H), 7.55−7.48 (m, 3H), 7.33 (dd, J = 7.8, 1.2 Hz, 1H), 6.43 (d, J = 15.6 Hz, 1H), 3.77 (s, 3H), 3.41 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 166.7, 141.6, 139.4, 131.0, 130.6, 129.4, 128.1, 126.0, 121.3, 52.0, 36.0. IR (neat): 1716, 1638, 1437, 1321, 1291, 1195, 1172, 1073, 978, 960, 764 cm^{-1}. HRMS (ESI): m/z calcd for $C_{11}H_{12}N_2O_3$ $[M + Na]^+$, 243.0740; found, 243.0749.

For the scale-up reaction, a flame-dried 25 mL flask was charged with *N*-alkyl aniline derivatives (2.0 mmol), catalyst ***o*-NQ** (0.20 mmol, 10 mol %), and 2-nitropropane (20 mmol). The solution was stirred under O_2 at 120 °C. After the reaction was complete by TLC (24 h), the reaction mixture was then cooled to room temperature. $[RhCp^*Cl_2]_2$ (0.030 mmol, 3 mol %), AgOAc (0.60 mmol, 60 mol %), and methylacrylate (1.0 mmol) in ethanol (0.75 mL) were added to the vial. The mixture was stirred at 60 °C under O_2 for 18 h. Upon the complete consumption of alkene, the reaction was cooled to room temperature. Volatile solvent and reagents were removed by rotary evaporation, and the residue was purified by silica gel flash chromatography using hexane/EtOAc (50:1) to afford the *N*-nitroso alkenylated **5a** in 72% yield (158 mg).

*(E)-Methyl 3-(2-(Ethyl(nitroso)amino)phenyl)acrylate (**5b**).* Eluent: 50:1 hexanes/ethyl acetate; 45 mg, 95% yield, yellow crystalline solid. The product was prepared via the general procedure B. The title compound was obtained as an inseparable mixture of *syn*- and *anti*-isomers due to the different conformations of the N═O bond (1:0.39). ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9a] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.76 (dd, J = 7.8, 1.2 Hz, 1H), 7.73 (dd, J = 7.8, 1.2 Hz, 0.39H), 7.55−7.50 (m, 2.63H), 7.49−7.45 (m, 0.85H), 7.31 (dd, J = 7.8, 1.2 Hz, 1H), 7.21 (d, J = 16.8 Hz, 0.35H), 6.99 (dd, J = 7.8, 1.8 Hz, 0.39H), 6.44 (d, J = 15.6 Hz, 1.12H), 6.40 (d, J = 16.2 Hz, 0.20H), 4.55 (bro, 0.71H), 3.98 (q, J = 7.2 Hz, 1.91H), 3.78 (s, 3.08H), 3.77 (s, 1.02H), 1.39 (t, J = 7.2 Hz, 1.17H), 1.09 (t, J = 7.2 Hz, 2.93H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 166.7, 140.3, 139.4, 138.9, 137.8, 132.4, 131.6, 131.2, 131.0, 130.0, 129.7, 128.1, 127.6, 127.4, 127.4, 121.4, 121.2, 52.0(3), 51.9(9), 49.4, 42.7, 14.3, 11.3.

*(E)-Methyl 3-(2-(Isopropyl(nitroso)amino)phenyl)acrylate (**5c**).* Eluent: 50:1 hexanes/ethyl acetate; 34 mg, 69% yield, yellow crystalline solid. The product was prepared via the general procedure B. The title compound was obtained as an inseparable mixture of *syn*- and *anti*-isomers due to the different conformations of the N═O bond (1:0.5). ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9a] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.81−7.79 (m, 0.5H), 7.74−7.72 (m, 1H), 7.57−7.51 (m, 1H), 7.49−7.44 (m, 2H), 7.30−7.28 (m, 0.5H), 7.21 (d, J = 15.6 Hz, 1H), 6.98−6.95 (m, 1H), 6.44 (d, J = 15.6 Hz, 0.5H), 6.39 (d, J = 15.6 Hz, 1H), 5.15 (septet, J = 7.2 Hz, 0.5H), 4.93 (septet, J = 7.2 Hz, 1H), 3.76 (s, 4.5H), 1.59 (d, J = 7.2 Hz, 3H), 1.44 (d, J = 7.2 Hz, 3H), 1.12 (d, J = 6.6 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 166.6(9), 166.6(6), 139.7, 139.4, 138.5, 137.5, 133.6, 132.8, 131.0, 130.7, 130.0, 129.1, 128.2, 127.7, 127.2, 121.2, 120.9, 57.1, 52.0, 47.9, 22.8, 21.7, 19.6.

*(E)-Methyl 3-(5-Methyl-2-(methyl(nitroso)amino)phenyl)acrylate (**5d**).* Eluent: 50:1 hexanes/ethyl acetate; 44 mg, 93% yield, yellow crystalline solid. The product was prepared via the general procedure B. The title compound was obtained as an inseparable mixture of *syn*- and *anti*-isomers due to the different conformations of the N═O bond (1:0.1). ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9a] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.53 (bro, 1H), 7.50 (d, J = 15.6 Hz, 1H), 7.32 (dd, J = 7.2, 1.2 Hz, 1H), 7.21 (d, J = 9.8 Hz, 1H), 6.41 (m, d, J = 15.6 Hz, 1H), 3.76 (s, 3H), 3.38 (s, 3H), 2.43 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 166.7, 139.6, 139.5, 139.3, 131.8, 130.3, 128.5, 126.0, 121.0, 52.0, 36.1, 21.3.

*Methyl (E)-3-(5-Methoxy-2-(methyl(nitroso)amino)phenyl)-acrylate (**5e**).* Eluent: 40:1 hexanes/ethyl acetate; 18 mg, 35% yield, yellow crystalline solid. The product was prepared via the general procedure B. The title compound was obtained as an inseparable mixture of *syn*- and *anti*-isomers due to the different conformations of the N═O bond (1:0.12). ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9a] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.46 (d, J = 15.6 Hz, 1H), 7.23 (d, J = 9.0 Hz, 1H), 7.19 (d, J = 2.4 Hz, 1H), 7.16 (d, J = 2.4 Hz, 0.12H), 7.12 (d, J = 15.6 Hz, 0.12H), 7.03 (dd, J = 9.0, 2.4 Hz, 1H), 7.03 (dd, J = 9.0, 2.4 Hz, 0.12H), 6.91 (d, J = 9.0 Hz, 0.12H), 6.40 (d, J = 15.6 Hz, 1H), 6.36 (d, J = 16.8 Hz, 0.12H), 4.07 (s, 0.36H), 3.87 (s, 3H), 3.83 (s, 0.36), 3.76 (s, 3H), 3.75 (s, 0.36H), 3.36 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 166.6(3), 166.5(9), 160.4, 160.1, 139.2, 138.7, 134.9, 132.8, 132.2, 131.9, 127.7, 127.6, 121.5, 121.3, 117.2, 116.7, 112.4, 112.0, 55.8, 55.7, 52.0, 41.5, 36.3, 35.5.

*Methyl (E)-3-(5-Fluoro-2-(methyl(nitroso)amino)phenyl)acrylate (**5f**).* Eluent: 50:1 hexanes/ethyl acetate; 43 mg, 90% yield, yellow amorphous solid. The product was prepared via the general procedure B. The title compound was obtained as an inseparable mixture of *syn*- and *anti*-isomers due to the different conformations of the N═O bond (1:0.12). ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9a] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.45 (dd, J = 15.6, 1.2 Hz, 1H), 7.42 (dd, J = 9.0, 3.0 Hz, 1H), 7.38 (dd, J = 9.0, 3.0 Hz, 0.12H), 7.32 (dd, J = 9.0, 4.8 Hz, 1H), 7.22 (dt, J = 9.0, 3.0 Hz, 1H), 7.19−7.15 (m, 0.19H), 7.09 (dd, J = 9.6, 1.2 Hz, 0.12H), 7.00 (dd, J = 9.0, 4.8 Hz, 0.12H), 6.42 (d, J = 16.2 Hz, 1H), 6.38 (d, J = 16.2 Hz, 0.12H), 4.10 (s, 0.36H), 3.78 (s, 3H), 3.77 (s, 0.36H), 3.38 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 166.3, 163.0 (C−F, $^1J_{C-F}$ = 207.0 Hz), 162.9 (C−F, $^1J_{C-F}$ = 207.0 Hz), 138.2, 137.9, 137.8, 137.5, 135.0, 134.1 (C−F, $^2J_{C-F}$ = 15.6 Hz), 132.9 (C−F, $^3J_{C-F}$ = 7.1 Hz), 128.6 (C−F, $^2J_{C-F}$ = 20.4 Hz), 128.1 (C−F, $^3J_{C-F}$ = 7.3 Hz), 122.5, 122.4, 118.5 (C−F, $^2J_{C-F}$ = 19.1 Hz), 118.0 (C−F, $^2J_{C-F}$ = 19.1 Hz), 114.5 (C−F, $^2J_{C-F}$ = 19.1 Hz), 114.1 (C−F, $^2J_{C-F}$ = 19.1 Hz), 52.1, 41.3, 36.1.

*Methyl (E)-3-(5-Chloro-2-(methyl(nitroso)amino)phenyl)acrylate (**5g**).* Eluent: 50:1 hexanes/ethyl acetate; 42 mg, 83% yield, yellow amorphous solid, mp 130−132 °C. The product was prepared via the general procedure B. The title compound was obtained as an inseparable mixture of *syn*- and *anti*-isomers due to the different conformations of the N═O bond (1:0.11). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.70 (d, J = 1.8 Hz, 1H), 7.67 (d, J = 2.4 Hz, 0.11H), 7.48 (dd, J = 8.4, 2.4 Hz, 1H), 7.46 (d, J = 16.2 Hz, 1H), 7.28 (d, J = 8.4 Hz, 1H), 7.08 (d, J = 15.6 Hz, 0.11H), 6.96 (d, J = 8.4 Hz, 0.11H), 6.43 (d, J = 15.6 Hz, 1H), 6.39 (d, J = 16.2 Hz, 0.11H), 4.10 (s, 0.33), 3.78 (s, 3H), 3.77 (s, 0.33H), 3.38 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 160.3, 140.0, 138.2, 137.4, 137.3, 136.1, 135.3, 133.6, 132.1, 131.3, 130.9, 128.0, 127.4, 127.2, 122.5, 52.2, 41.1, 35.9. IR (neat): 1703, 1491, 1450, 1433, 1413, 1288, 1249, 1197, 1105, 1071, 1031, 967, 909, 859, 834, 820 cm^{-1}. HRMS (ESI): m/z calcd for $C_{11}H_{11}ClN_2O_3$ $[M + H]^+$, 255.0531; found, 255.0539.

*Methyl (E)-3-(5-Bromo-2-(methyl(nitroso)amino)phenyl)acrylate (**5h**).* Eluent: 50:1 hexanes/ethyl acetate; 25 mg, 42% yield, yellow crystalline solid, mp 120−121 °C. The product was prepared via the general procedure B. The title compound was obtained as an inseparable mixture of *syn*- and *anti*-isomers due to the different conformations of the N═O bond (1:0.14). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.87 (d, J = 2.4 Hz, 1H), 7.83 (d, J = 1.8 Hz, 0.14H), 7.64 (dd, J = 8.4, 2.4 Hz, 1H), 7.59 (dd, J = 8.4, 2.4 Hz, 0.14H), 7.46 (d, J = 15.6 Hz, 1H), 7.21 (d, J = 2.4 Hz, 1H), 7.08 (d, J = 16.2 Hz, 0.14H), 6.90 (d, J = 3.0 Hz, 0.14H), 6.43 (d, J = 15.6 Hz, 1H), 6.40 (d, J = 16.2 Hz, 0.14H), 4.10 (s, 0.42H), 3.79 (s, 3H), 3.78 (s, 0.42H), 3.38 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 166.3, 140.6, 138.1, 137.3, 134.3, 133.9, 132.4, 131.0, 128.1, 127.3, 123.2, 122.9, 122.5, 51.2, 41.1, 35.8. IR (neat): 1716, 1638, 1485, 1437, 1340, 1314, 1286, 1262, 1195, 1168, 1092, 1068, 984, 870, 818, 755 cm^{-1}. HRMS (ESI): m/z calcd for $C_{11}H_{11}BrN_2O_3$ $[M + H]^+$, 299.0025; found, 299.0018.

*Methyl (E)-3-(2-(Methyl(nitroso)amino)-5-(trifluoromethyl)-phenyl)acrylate (**5i**).* Eluent: 40:1 hexanes/ethyl acetate; 47 mg, 81% yield, yellow crystalline solid, mp 110−112 °C. The product was prepared via the general procedure B. The title compound was obtained as an inseparable mixture of *syn*- and *anti*-isomers due to the

https://dx.doi.org/10.1021/acs.joc.0c02776
J. Org. Chem. XXXX, XXX, XXX−XXX

different conformations of the N═O bond (1:0.08). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.98 (d, J = 1.8 Hz, 1H), 7.78 (dd, J = 8.4, 1.2 Hz, 1H), 7.56 (d, J = 15.6 Hz, 1H), 7.48 (d, J = 8.4 Hz, 1H), 6.51 (d, J = 15.6 Hz, 1H), 3.80 (s, 3H), 3.43 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 166.3, 144.1, 138.4, 131.5 (C−F, $^2J_{C-F}$ = 27.5 Hz), 131.1, 127.6 (C−F, $^3J_{C-F}$ = 3.6 Hz), 126.0, 125.5 (C−F, $^3J_{C-F}$ = 3.6 Hz), 123.4 (C−F, $^1J_{C-F}$ = 229.9 Hz), 122.9, 52.2, 35.6. ^{19}F NMR ($CDCl_3$, 564 MHz): δ −62.7. IR (neat): 1716, 1642, 1620, 1441, 1314, 1295, 1271, 1161, 1122, 1088, 988, 895, 872, 837 cm^{-1}. HRMS (ESI): m/z calcd for $C_{12}H_{11}F_3N_2O_3$ [M + K]$^+$, 327.0353; found, 327.0360.

Methyl (E)-3-(3-Methoxy-3-oxoprop-1-en-1-yl)-4-(methyl(nitroso)amino)benzoate (**5j**). Eluent: 30:1 hexanes/ethyl acetate; 49 mg, 88% yield, yellow crystalline solid, mp 121−123 °C. The product was prepared via the general procedure B. The title compound was obtained as an inseparable mixture of *syn*- and *anti*-isomers due to the different conformations of the N═O bond (1:0.07). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.41 (d, J = 1.8 Hz, 1H), 8.16 (dd, J = 8.4, 1.8 Hz, 1H), 7.55 (d, J = 16.2 Hz, 1H), 7.42 (d, J = 7.8 Hz, 1H), 6.40 (d, J = 15.6 Hz, 1H), 3.97 (s, 3H), 3.79 (s, 3H), 3.42 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 166.5, 165.7, 144.8, 138.9, 131.8, 130.8, 130.4, 129.8, 125.3, 122.2, 52.8, 52.1, 35.6. IR (neat): 1716, 1640, 1610, 1437, 1282, 1256, 1198, 1167, 1113, 1068, 982, 962, 874, 807, 770, 753 cm^{-1}. HRMS (ESI): m/z calcd for $C_{13}H_{14}N_2O_5$ [M + Na]$^+$, 301.0794; found, 301.0801.

Methyl (E)-3-(5-Acetyl-2-(methyl(nitroso)amino)phenyl)acrylate (**5k**). Eluent: 40:1 hexanes/ethyl acetate; 36 mg, 68% yield, yellow crystalline solid, mp 104−107 °C. The product was prepared via the general procedure B. The title compound was obtained as an inseparable mixture of *syn*- and *anti*-isomers due to the different conformations of the N═O bond (1:0.08). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.30 (d, J = 1.8 Hz, 1H), 8.08 (dd, J = 8.4, 1.8 Hz, 1H), 7.57 (d, J = 16.2 Hz, 1H), 7.45 (d, J = 8.4 Hz, 1H), 6.53 (d, J = 15.6 Hz, 1H), 3.79 (s, 3H), 3.42 (s, 3H), 2.67 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 196.4, 166.5, 144.8, 139.1, 137.2, 130.5, 128.5, 125.5, 122.3, 52.1, 35.6, 26.8. IR (neat): 1709, 1687, 1638, 1603, 1439, 1329, 1282, 1245, 1195, 1176, 1094, 1059, 982, 876, 840, 816, 755 cm^{-1}. HRMS (ESI): m/z calcd for $C_{13}H_{14}N_2O_4$ [M + H]$^+$, 263.1026; found, 263.1017.

Methyl (E)-3-(4-(Methyl(nitroso)amino)-[1,1′-biphenyl]-3-yl)-acrylate (**5l**). Eluent: 40:1 hexanes/ethyl acetate; 26 mg, 44% yield, yellow crystalline solid, mp 110−112 °C. The product was prepared via the general procedure B. The title compound was obtained as an inseparable mixture of *syn*- and *anti*-isomers due to the different conformations of the N═O bond (1:0.08). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.93 (d, J = 2.4 Hz, 1H), 7.73 (dd, J = 8.4, 2.4 Hz, 1H), 7.64−7.59 (m, 3H), 7.50 (t, J = 7.2 Hz, 2H), 7.45−7.42 (m, 1H), 7.42 (d, J = 8.4 Hz, 2H), 6.52 (d, J = 9.6 Hz, 1H), 3.80 (s, 3H), 3.45 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 166.7, 142.6, 140.7, 139.6, 139.4, 130.8, 129.7, 129.5, 129.2(4), 129.1(8), 128.4, 127.3, 127.0, 126.8, 126.3, 121.6, 121.5, 52.1, 36.0. IR (neat): 1703, 1438, 1403, 1273, 1247, 1183, 1079, 1040, 993, 964, 835, 759, 699 cm^{-1}. HRMS (ESI): m/z calcd for $C_{17}H_{16}N_2O_3$ [M + Na]$^+$, 319.1053; found, 319.1051.

Methyl (E)-3-(4-Methyl-2-(methyl(nitroso)amino)phenyl)acrylate (**5m**). Eluent: 50:1 hexanes/ethyl acetate; 45 mg, 95% yield, yellow crystalline solid. The product was prepared via the general procedure B. The title compound was obtained as an inseparable mixture of *syn*- and *anti*-isomers due to the different conformations of the N═O bond (1:0.1). ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9a] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.64 (d, J = 9.0 Hz, 1H), 7.50 (d, J = 16.2 Hz, 1H), 7.29 (d, J = 7.8 Hz, 1H), 7.14 (s, 1H), 6.39 (d, J = 15.6 Hz, 1H), 3.77 (s, 3H), 3.39 (s, 3H), 2.43 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 166.9, 141.9, 141.5, 139.3, 130.3, 127.9, 127.7, 127.3, 126.7, 120.3, 51.9, 36.1, 21.4.

tert-Butyl (E)-3-(2-(Methyl(nitroso)amino)phenyl)acrylate (**5n**). Eluent: 50:1 hexanes/ethyl acetate; 37 mg, 70% yield, yellow liquid. The product was prepared via the general procedure B. The title compound was obtained as an inseparable mixture of *syn*- and *anti*-isomers due to the different conformations of the N═O bond (1:0.4). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.74 (dd, J = 8.4, 1.8 Hz, 1H), 7.51−7.42 (m, 3H+1.2H), 7.32 (dd, J = 7.8, 1.8 Hz, 1H+0.4H), 6.84 (d, J = 12.6 Hz, 0.4H), 6.37 (d, J = 16.2 Hz, 1H), 5.96 (d, J = 12.0 Hz, 0.4H), 3.40 (s, 3H), 3.35 (s, 1.2 H), 1.50 (s, 9H), 1.32 (s, 3.6H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 165.5, 164.9, 141.6, 140.5, 138.4, 138.0, 137.3, 132.2, 131.1, 130.8(1), 130.7(5), 130.5, 130.0, 129.4, 129.2, 128.4, 128.0, 127.4, 126.2, 125.0, 124.7, 123.6, 123.5, 81.1, 36.1, 35.4, 28.2, 28.0. IR (neat): 1705, 1638, 1442, 1370, 1323, 1295, 1148, 1074, 1045, 978, 958, 762 cm^{-1}. HRMS (ESI): m/z calcd for $C_{14}H_{18}N_2O_3$ [M + Na]$^+$, 285.1209; found, 285.1214.

(E)-N-Methyl-N-(2-styrylphenyl)nitrous Amide (**5o**). Eluent: 50:1 hexanes/ethyl acetate; 38 mg, 80% yield, yellow liquid. The product was prepared via the general procedure B. The title compound was obtained as an inseparable mixture of *syn*- and *anti*-isomers due to the different conformations of the N═O bond (1:0.1). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.81 (d, J = 6.6 Hz, 1H), 7.49 (t, J = 7.8 Hz, 1H), 7.46 (d, J = 7.2 Hz, 2H), 7.43−7.40 (m, 1H), 7.38−7.34 (m, 2H), 7.33−7.28 (m, 2H), 7.13 (d, J = 16.2 Hz, 1H), 6.92 (d, J = 15.6 Hz, 1H), 3.42 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 140.5, 136.7, 133.6, 132.5, 129.6, 128.9, 128.8, 128.5(4), 128.4(9), 128.4, 127.1, 127.0, 126.9, 126.5, 123.0, 36.1. IR (neat): 1498, 1437, 1396, 1202, 1120, 1074, 962, 759, 691 cm^{-1}. HRMS (ESI): m/z calcd for $C_{15}H_{14}N_2O$ [M + H]$^+$, 239.1178; found, 239.1183.

N-(2′,5′-Dioxo-2′,5′-dihydro-[1,1′-biphenyl]-2-yl)-N-methylnitrous Amide (**5p**). Eluent: 30:1 hexanes/ethyl acetate; 29 mg, 60% yield, brown amorphous solid. The product was prepared via the general procedure B. ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[27] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.64−7.61 (m, 1H), 7.51 (t, J = 7.8 Hz, 1H), 7.43−7.41 (m, 1H), 7.37 (d, J = 7.2 Hz, 1H), 6.86 (d, J = 2.4 Hz, 1H), 6.77 (dd, J = 10.2, 2.4 Hz, 1H), 6.70 (d, J = 9.6 Hz, 1H), 3.40 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 187.2, 185.4, 147.0, 141.2, 136.8, 136.4, 134.6, 131.3, 131.1, 128.8, 128.6, 123.1, 34.8.

N-Methyl-N-(4′-methyl-2′,5′-dioxo-2′,5′-dihydro-[1,1′-biphenyl]-2-yl)nitrous Amide (**5q**). Eluent: 30:1 hexanes/ethyl acetate; 44 mg, 88% yield, brown gum. The product was prepared via the general procedure B. The title compound was obtained as an inseparable mixture of regioisomers (1:0.51). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.62−7.58 (m, 1.5H), 7.48 (dt, J = 7.8, 1.8 Hz, 1.43H), 7.41−7.38 (m, 1.61H), 7.37−7.34 (m, 1.44H), 6.83 (s, 0.91H), 6.77 (d, J = 3.0 Hz, 1.00H), 6.60−6.59 (m, 1.13H), 6.52 (d, J = 1.2 Hz, 1.83H), 3.39 (s, 5.42H), 3.38 (s, 3.17H), 2.04 (d, J = 1.2 Hz, 5.84H), 1.98 (d, J = 1.2 Hz, 3.00H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 187.7, 187.1, 186.1, 185.6, 147.0, 146.8, 146.3, 145.8, 141.2, 141.1, 134.6, 134.5, 133.6, 133.3, 133.1, 131.3, 131.2, 131.0, 129.7, 129.2, 128.8, 128.6, 123.1, 35.0, 34.9, 16.3, 15.7. IR (neat): 1709, 1687, 1599, 1437, 1361, 1327, 1245, 1193, 1172, 1094, 1060, 984, 844, 818, 755 cm^{-1}. HRMS (ESI): m/z calcd for $C_{14}H_{12}N_2O_3$ [M + Na]$^+$, 279.0740; found, 279.0740.

N-(2-(1,4-Dioxo-1,4-dihydronaphthalen-2-yl)phenyl)-N-methylnitrous Amide (**5r**). Eluent: 30:1 hexanes/ethyl acetate; 41 mg, 70% yield, brown amorphous solid, mp 122−124 °C. The product was prepared via the general procedure B. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.07 (dd, J = 7.2, 1.2 Hz, 1H), 7.99 (dd, J = 7.2, 1.2 Hz, 1H), 7.76−7.71 (m, 2H), 7.63 (dt, J = 7.8, 1.8 Hz, 1H), 7.53 (dt, J = 7.8, 1.8 Hz, 1H), 7.48 (dd, J = 7.8, 1.8 Hz, 1H), 7.40 (d, J = 9.0 Hz, 1H), 7.07 (s, 1H), 3.43 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 184.8, 183.5, 148.9, 141.3, 137.1, 134.2, 134.0, 132.2, 131.8, 131.4, 131.0, 129.5, 128.6, 127.1, 126.3, 123.3, 34.9. IR (neat): 1668, 1655, 1614, 1593, 1497, 1456, 1353, 1332, 1280, 1254, 1195, 1085, 1053, 964, 926, 781, 760, 710 cm^{-1}. HRMS (ESI): m/z calcd for $C_{17}H_{12}N_2O_3$ [M + H]$^+$, 293.0920; found, 293.0926.

N-(2-(1,4-Dioxo-1,4-dihydronaphthalen-2-yl)-5-methylphenyl)-N-methylnitrous Amide (**5s**). Eluent: 30:1 hexanes/ethyl acetate; 31 mg, 51% yield, brown amorphous solid, mp 180−182 °C. The product was prepared via the general procedure B. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.08−8.06 (m, 1H), 7.98 (dd, J = 7.2, 1.2 Hz, 1H), 7.75−7.68 (m, 2H), 7.37 (d, J = 8.4 Hz, 1H), 7.33 (d, J = 8.4 Hz,

https://dx.doi.org/10.1021/acs.joc.0c02776
J. Org. Chem. XXXX, XXX, XXX−XXX

1H), 7.21 (bro, 1H), 7.05 (s, 1H), 3.42 (s, 3H), 2.50 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 184.8, 183.6, 148.9, 141.6, 141.2, 136.8, 134.1, 134.0, 132.2, 131.9, 1312, 129.4, 127.0, 126.3, 123.9, 35.0, 21.5. IR (neat): 1657, 1593, 1441, 1413, 1398, 1292, 1275, 1248, 1232, 1206, 1087, 1046, 1021, 893, 837, 783, 751, 714 cm^{-1}. HRMS (ESI): m/z calcd for $C_{18}H_{14}N_2O_3$ $[M + H]^+$, 307.1077; found, 307.1083.

*N-(4-Chloro-2-(1,4-dioxo-1,4-dihydronaphthalen-2-yl)phenyl)-N-methylnitrous Amide (**5t**).* Eluent: 30:1 hexanes/ethyl acetate; 24 mg, 37% yield, brown gum. The product was prepared via the general procedure B. ^1H NMR ($CDCl_3$, 600 MHz): δ 8.08 (dd, J = 7.2, 1.2 Hz, 1H), 7.99 (dd, J = 7.2, 1.2 Hz, 1H), 7.77−7.72 (m, 2H), 7.60 (dd, J = 8.4, 3.0 Hz, 1H), 7.48 (d, J = 3.0 Hz, 1H), 7.34 (d, J = 8.4 Hz, 1H), 7.07 (s, 1H), 3.40 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 184.4, 183.1, 147.6, 139.9, 137.4, 134.4, 134.3, 134.2, 132.1, 131.7, 131.3, 131.0, 130.9, 127.1, 126.5, 124.5, 34.8. IR (neat): 1657, 1593, 1493, 1452, 1398, 1344, 1306, 1273, 1251, 1191, 1105, 1079, 1049, 1025, 958, 891, 818, 781, 744, 716, 669 cm^{-1}. HRMS (ESI): m/z calcd for $C_{17}H_{11}ClN_2O_3$ $[M + H]^+$, 327.0531; found, 327.0538.

General Procedure C: Denitrosation of *N*-Nitrosamines. *N*-Nitrosamine (1.0 equiv) was stirred in dichloromethane for approximately 2 min at room temperature after the addition of iodine (0.3 equiv) and triethylsilane (1.5 equiv). The reaction was further allowed to stir for 10 min, and the progress of the reaction was monitored by TLC. After the complete consumption of *N*-nitrosoamine, the reaction mixture was quenched with a saturated solution of sodium thiosulfate (20 mL) extracted with ethyl acetate (2 × 25 mL). The organic layer was dried over anhydrous sodium sulfate, concentrated, and subjected to column chromatography using hexanes/ethyl acetate (20:1) to obtain the corresponding substituted secondary amines.

*Methyl (E)-3-(2-(Methylamino)phenyl)acrylate (**6a**).* Eluent: 20:1 hexanes/ethyl acetate; 31 mg, 81% yield, yellow crystalline solid. The product was prepared via the general procedure C. ^1H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9a] ^1H NMR ($CDCl_3$, 600 MHz): δ 7.83 (d, J = 15.6 Hz, 1H), 7.37 (dd, J = 7.8, 1.2 Hz, 1H), 7.31−7.27 (m, 1H), 6.73 (t, J = 7.8 Hz, 1H), 6.67 (d, J = 7.8 Hz, 1H), 6.34 (d, J = 15.6 Hz, 1H), 4.24 (bro, 1H), 3.80 (s, 3H), 2.89 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 167.8, 147.7, 140.5, 131.7, 128.2, 119.9, 117.8, 117.4, 111.0, 51.7, 30.7.

*Methyl (E)-3-(2-(Ethylamino)phenyl)acrylate (**6b**).* Eluent: 20:1 hexanes/ethyl acetate; 35 mg 86% yield, yellow crystalline solid. The product was prepared via the general procedure C. ^1H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9a] ^1H NMR ($CDCl_3$, 600 MHz): δ 7.83 (d, J = 15.6 Hz, 1H), 7.36 (dd, J = 7.8, 1.8 Hz, 1H), 7.27−7.23 (m, 1H), 6.70 (t, J = 7.8 Hz, 1H), 6.67 (d, J = 8.4 Hz, 1H), 6.33 (d, J = 16.2 Hz, 1H), 3.79 (s, 3H), 3.19 (q, J = 7.2 Hz, 2H), 1.30 (t, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 167.9, 146.8, 140.5, 131.7, 128.3, 119.7, 117.8, 117.3, 111.6, 51.7, 38.6, 14.8.

*Methyl (E)-3-(2-(Isopropylamino)phenyl)acrylate (**6c**).* Eluent: 20:1 hexanes/ethyl acetate; 23 mg, 52% yield, yellow crystalline solid. The product was prepared via the general procedure C. ^1H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9a] ^1H NMR ($CDCl_3$, 600 MHz): δ 7.81 (d, J = 16.2 Hz, 1H), 7.36 (dd, J = 7.8, 1.8 Hz, 1H), 7.27−7.23 (m, 1H), 6.70−6.67 (m, 1H), 6.33 (d, J = 15.6 Hz, 1H), 3.81 (s, 3H), 3.70 (septet, J = 6.0 Hz, 1H), 1.26 (d, J = 6.0 Hz, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 167.9, 146.0, 140.6, 131.6, 128.5, 119.8, 117.8, 117.0, 112.2, 51.7, 44.4, 23.1.

*Methyl (E)-3-(5-Methyl-2-(methylamino)phenyl)acrylate (**6d**).* Eluent: 20:1 hexanes/ethyl acetate; 31 mg, 75% yield, yellow crystalline solid. The product was prepared via the general procedure C. ^1H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9a] ^1H NMR ($CDCl_3$, 600 MHz): δ 7.82 (d, J = 15.0 Hz, 1H), 7.19 (d, J = 1.8 Hz, 1H), 7.11 (dd, J = 8.4, 2.4 Hz, 1H), 6.62 (d, J = 8.4 Hz, 1H), 6.33 (d, J = 15.0 Hz, 1H), 3.80 (s, 3H), 2.87 (s, 3H), 2.25 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 167.9, 145.5, 140.5, 132.5, 128.6, 126.7, 120.0, 117.7, 111.6, 51.7, 31.1, 20.4.

*Methyl (E)-3-(5-Methoxy-2-(methylamino)phenyl)acrylate (**6e**).* Eluent: 20:1 hexanes/ethyl acetate; 13 mg, 30% yield, yellow crystalline solid. The product was prepared via the general procedure C. ^1H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9a] ^1H NMR ($CDCl_3$, 600 MHz): δ 7.81 (d, J = 16.2 Hz, 1H), 6.95 (d, J = 3.0 Hz, 1H), 6.92 (dd, J = 8.4, 3.0 Hz, 1H), 6.40 (d, J = 8.4 Hz, 1H), 6.33 (d, J = 16.2 Hz, 1H), 3.80 (s, 3H), 3.77 (s, 3H), 2.87 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 167.8, 151.9, 142.6, 140.3, 120.8, 118.4, 118.2, 112.7(5), 112.6(9), 56.0, 51.8, 31.4.

*Methyl (E)-3-(5-Fluoro-2-(methylamino)phenyl)acrylate (**6f**).* Eluent: 20:1 hexanes/ethyl acetate; 29 mg, 69% yield, yellow crystalline solid. The product was prepared via the general procedure C. ^1H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9a] ^1H NMR ($CDCl_3$, 600 MHz): δ 7.76 (d, J = 16.8 Hz, 1H), 7.08 (dd, J = 9.6, 2.4 Hz, 1H), 7.00 (dt, J = 9.0, 2.4 Hz, 1H), 6.61 (dd, J = 9.0, 3.6 Hz, 1H), 6.31 (d, J = 15.6 Hz, 1H), 3.80 (s, 3H), 2.86 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 167.5, 156.4 (C−F, $^1J_{C-F}$ = 195.0 Hz), 144.1, 139.2, 121.0 (C−F, $^3J_{C-F}$ = 6.0 Hz), 119.2, 118.4 (C−F, $^2J_{C-F}$ = 18.0 Hz), 114.0 (C−F, $^2J_{C-F}$ = 19.1 Hz), 112.4 (C−F, $^3J_{C-F}$ = 4.8 Hz), 51.9, 31.3. ^{19}F NMR ($CDCl_3$, 564 MHz): δ −127.6.

*Methyl (E)-3-(5-Chloro-2-(methylamino)phenyl)acrylate (**6g**).* Eluent: 20:1 hexanes/ethyl acetate; 33 mg, 72% yield, yellow crystalline solid. The product was prepared via the general procedure C. ^1H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[28] ^1H NMR ($CDCl_3$, 600 MHz): δ 7.72 (d, J = 15.6 Hz, 1H), 7.31 (d, J = 1.8 Hz, 1H), 7.21 (dd, J = 9.0, 2.4 Hz, 1H), 6.60 (d, J = 9.0 Hz, 1H), 6.32 (d, J = 16.2 Hz, 1H), 3.80 (s, 3H), 2.87 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 167.4, 145.9, 138.9, 131.3, 127.5, 122.5, 121.3, 119.3, 112.6, 51.9, 31.0.

*Methyl (E)-3-(5-Bromo-2-(methylamino)phenyl)acrylate (**6h**).* Eluent: 20:1 hexanes/ethyl acetate; 20 mg, 37% yield, yellow crystalline solid. The product was prepared via the general procedure C. ^1H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[28] ^1H NMR ($CDCl_3$, 600 MHz): δ 7.68 (d, J = 15.6 Hz, 1H), 7.42 (d, J = 1.8 Hz, 1H), 7.32 (dd, J = 8.4, 2.4 Hz, 1H), 6.50 (d, J = 9.0 Hz, 1H), 6.30 (d, J = 15.0 Hz, 1H), 4.15 (bro, 1H), 3.78 (s, 3H), 2.84 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 167.4, 146.6, 138.9, 134.0, 130.2, 121.5, 119.0, 112.5, 109.0, 51.8, 30.7.

*Methyl (E)-3-(2-(Methylamino)-5-(trifluoromethyl)phenyl)-acrylate (**6i**).* Eluent: 20:1 hexanes/ethyl acetate; 34 mg, 65% yield, yellow crystalline solid, mp 66−68 °C. The product was prepared via the general procedure C. ^1H NMR ($CDCl_3$, 600 MHz): δ 7.74 (d, J = 15.6 Hz, 1H), 7.56 (d, J = 1.8 Hz, 1H), 7.49 (dd, J = 8.4, 1.8 Hz, 1H), 6.67 (d, J = 8.4 Hz, 1H), 6.38 (d, J = 15.6 Hz, 1H), 4.39 (bro, 1H), 3.82 (s, 3H), 2.93 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 167.4, 149.7, 139.1, 128.4 (C−F, $^3J_{C-F}$ = 2.5 Hz), 125.5 (C−F, $^1J_{C-F}$ = 225.0 Hz), 125.3 (C−F, $^3J_{C-F}$ = 3.6 Hz), 119.8, 119.3, 119.0 C−F, $^2J_{C-F}$ = 27.5 Hz), 110.3, 52.0, 30.5. ^{19}F NMR ($CDCl_3$, 564 MHz): δ −61.2. IR (neat): 3414, 1703, 1617, 1580, 1536, 1323, 1263, 1156, 1107, 977, 902, 861, 820 cm^{-1}. HRMS (ESI): m/z calcd for $C_{12}H_{12}F_3NO_2$ $[M + H]^+$, 260.0892; found, 260.0888.

*Methyl (E)-3-(3-Methoxy-3-oxoprop-1-en-1-yl)-4-(methylamino)benzoate (**6j**).* Eluent: 20:1 hexanes/ethyl acetate; 39 mg, 79% yield, yellow crystalline solid, mp 75−77 °C. The product was prepared via the general procedure C. Yellow solid. ^1H NMR ($CDCl_3$, 600 MHz): δ 8.01 (d, J = 2.4 Hz, 1H), 7.90 (dd, J = 8.4, 1.8 Hz, 1H), 7.72 (d, J = 16.2 Hz, 1H), 6.58 (d, J = 8.4 Hz, 1H), 6.38 (d, J = 15.6 Hz, 1H), 3.84 (s, 3H), 3.76 (s, 3H), 2.90 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ 167.5, 167.0, 150.8, 139.3, 133.1, 130.0, 119.1, 118.8, 118.3, 109.8, 51.8 51.7, 30.4. IR (neat): 3047, 1692, 1607, 1528, 1435, 1349, 1293, 1245, 1197, 1152, 999, 973, 854, 746 cm^{-1}. HRMS (ESI): m/z calcd for $C_{13}H_{15}NO_4$ $[M + H]^+$, 250.1073; found, 250.1071.

https://dx.doi.org/10.1021/acs.joc.0c02776
J. Org. Chem. XXXX, XXX, XXX−XXX

*Methyl (E)-3-(5-Acetyl-2-(methylamino)phenyl)acrylate (**6k**).* Eluent: 20:1 hexanes/ethyl acetate; 19 mg, 40% yield, yellow crystalline solid, mp 74−76 °C. The product was prepared via the general procedure C. Yellow solid. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.99 (d, J = 2.4 Hz, 1H), 7.91 (dd, J = 7.8, 1.8 Hz, 1H), 7.75 (d, J = 15.6 Hz, 1H), 6.64 (d, J = 7.8 Hz, 1H), 6.42 (d, J = 15.0 Hz, 1H), 4.66 (bro, 1H), 3.81 (s, 3H), 2.97 (d, J = 4.8 Hz, 3H), 2.52 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 196.3, 167.5, 151.0, 139.4, 132.5, 129.4, 126.6, 119.6, 118.9, 109.8, 52.0, 30.5, 26.2. IR (neat): 3336, 1715, 1603, 1551, 1431, 1349, 1293, 1256, 1163, 962, 857, 726 cm^{-1}. HRMS (ESI): m/z calcd for $C_{13}H_{15}NO_3$ [M + H]$^+$, 234.1124; found, 234.1121.

*Methyl (E)-3-(4-(Methylamino)-[1,1′-biphenyl]-3-yl)acrylate (**6l**).* Eluent: 20:1 hexanes/ethyl acetate; 21 mg, 40% yield, yellow crystalline solid, mp 110−112 °C. The product was prepared via the general procedure C. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.86 (d, J = 9.6 Hz, 1H), 7.62 (d, J = 1.8 Hz, 1H), 7.57−7.54 (m, 3H), 7.42 (t, J = 7.8 Hz, 2H), 7.31−7.28 (m, 1H), 6.75 (d, J = 7.8 Hz, 1H), 6.43 (d, J = 16.2 Hz, 1H), 4.20 (bro, 1H), 3.82 (s, 3H), 2.95 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 167.8, 147.2, 140.8, 140.5, 130.5, 130.3, 128.9, 126.8, 126.6, 126.5, 120.1, 118.3, 111.4, 51.8, 30.8. IR (neat): 3422, 1700, 1614, 1528, 1498, 1323, 1290, 1163, 988, 857, 816, 753, 690 cm^{-1}. HRMS (ESI): m/z calcd for $C_{17}H_{17}NO_2$ [M + H]$^+$, 268.1332; found, 268.1328.

*Methyl (E)-3-(4-Methyl-2-(methylamino)phenyl)acrylate (**6m**).* Eluent: 20:1 hexanes/ethyl acetate; 22 mg, 54% yield, yellow crystalline solid. The product was prepared via the general procedure C. ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[9a] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.80 (d, J = 16.2 Hz, 1H), 7.28 (d, J = 8.4 Hz, 1H), 6.55 (d, J = 8.4 Hz, 1H), 6.49 (s, 1H), 6.30 (d, J = 8.4 Hz, 1H), 3.79 (s, 3H), 2.88 (s, 3H), 2.33 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 168.1, 147.7, 142.4, 140.4, 128.3, 118.5, 117.2, 116.5, 111.7, 51.7, 30.8, 22.0.

*tert-Butyl (E)-3-(2-(Methylamino)phenyl)acrylate (**6n**).* Eluent: 20:1 hexanes/ethyl acetate; 24 mg, 52% yield, yellow liquid. The product was prepared via the general procedure C. ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[28] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.71 (d, J = 15.0 Hz, 1H), 7.36−7.33 (m, 1H), 7.29−7.26 (m, 1H), 6.70 (t, J = 7.2 Hz, 1H), 6.66 (d, J = 8.4 Hz, 1H), 6.26 (d, J = 16.2 Hz, 1H), 4.89 (bro, 1H), 2.88 (s, 3H), 1.54 (s, 9H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 166.8, 147.7, 139.3, 131.4, 128.3, 120.5, 120.2, 117.3, 110.8, 80.5, 30.7, 28.4.

*(E)-N-Methyl-2-styrylaniline (**6o**).* Eluent: 20:1 hexanes/ethyl acetate; 23 mg, 56% yield, yellow liquid. The product was prepared via the general procedure C. ^{1}H NMR and ^{13}C NMR spectra for this compound are consistent with previously reported literature data.[28] ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.53 (d, J = 7.8 Hz, 2H), 7.41 (dd, J = 7.8, 1.8 Hz, 1H), 7.38 (t, J = 7.8 Hz, 2H), 7.30−7.24 (m, 2H), 7.20 (d, J = 15.6 Hz, 1H), 6.99 (d, J = 16.2 Hz, 1H), 6.83 (t, J = 7.8 Hz, 1H), 6.76 (d, J = 8.4 Hz, 1H), 2.92 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 146.0, 137.7, 131.2, 129.1, 128.8, 127.7, 127.4, 127.0, 126.6, 124.6, 124.3, 118.4, 111.3, 31.4.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02776.

Experimental procedure and characterization data for all new compounds, and NMR spectra (PDF)

FAIR data, including the primary NMR FID files, for 1,2-di(naphthalen-1-yl)ethyne, 1,2-di(naphthalen-2-yl)-ethyne, 1,2-di(thiophen-3-yl)ethyne, 4,4′-(ethyne-1,2-diyl)dibenzonitrile, *N*-methyl-[1,1′-biphenyl]-4-amine, *N*-methylnaphthalen-2-amine, **3a**−**3zc**, **5a**−**5t**, and **6a**−**6o** (ZIP)

■ AUTHOR INFORMATION

Corresponding Authors

Hun Young Kim − *Department of Global Innovative Drugs, Chung-Ang University, Seoul 06974, Republic of Korea;* orcid.org/0000-0002-8461-8910; Email: hunnykim@cau.ac.kr

Kyungsoo Oh − *Center for Metareceptome Research, Graduate School of Pharmaceutical Sciences, Chung-Ang University, Seoul 06974, Republic of Korea;* orcid.org/0000-0002-4566-6573; Email: kyungsoooh@cau.ac.kr

Author

Tengda Si − *Center for Metareceptome Research, Graduate School of Pharmaceutical Sciences, Chung-Ang University, Seoul 06974, Republic of Korea*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.joc.0c02776

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This research was supported by the National Research Foundation of Korea (NRF) grant funded by the Korean government (MSICT) (NRF-2015R1A5A1008958 and NRF-2019R1A2C2089953).

■ REFERENCES

(1) (a) *The Chemistry of Anilines, Parts 1*−*2*; From the Patai Series: The Chemistry of Functional Groups Vol. and Series; Rappoport, Z., Ed.; John Wiley & Sons: Chichester, 2007. (b) Lamture, J. B. *Aniline and Its Analogs*; Notion Press: Chennai, India, 2018.

(2) Yi, C. S.; Yun, S. Y. Scope and Mechanistic Study of the Ruthenium-Catalyzed *ortho*-C−H Bond Activation and Cyclization Reactions of Arylamines with Terminal Alkynes. *J. Am. Chem. Soc.* **2005**, *127*, 17000−17006.

(3) Shi, A.; Zhang, C.; Li, S.; Pan, D.; Ding, S.; Cui, Y.; Jiao, N. Indoles from Simple Anilines and Alkynes: Palladium-Catalyzed C−H Activation Using Dioxygen as the Oxidant. *Angew. Chem., Int. Ed.* **2009**, *48*, 4572−4576.

(4) Midya, S. P.; Sahoo, M. K.; Landge, S. G.; Rajamohanan, P. R.; Balaraman, E. Reversed Reactivity of Anilines with Alkynes in the Rhodium-Catalyzed C−H Activation/Carbonylation Tandem. *Nat. Commun.* **2015**, *6*, 8591.

(5) For recent reviews, see: (a) Zhang, M.; Zhang, Y.; Jie, X.; Zhao, H.; Li, G.; Su, W. Recent Advances in Directed C−H Functionalizations Using Monodentate Nitrogen-Based Directing Groups. *Org. Chem. Front.* **2014**, *1*, 843−895. (b) Ros, A.; Fernandez, R.; Lassaletta, J. M. Functional Group Directed C−H Borylation. *Chem. Soc. Rev.* **2014**, *43*, 3229−3243. (c) Song, G.; Li, X. Substrate Activation Strategies in Rhodium(III)-Catalyzed Selective Functionalization of Arenes. *Acc. Chem. Res.* **2015**, *48*, 1007−1020. (d) Chen, Z.; Wang, B.; Zhang, J.; Yu, W.; Liu, Z.; Zhang, Y. Transition Metal-Catalyzed C−H Functionalization by the Use of Diverse Directing Groups. *Org. Chem. Front.* **2015**, *2*, 1107−1295. (e) Sambiagio, C.; Schönbauer, D.; Blieck, R.; Dao-Huy, T.; Pototschnig, G.; Schaaf, P.; Wiesinger, T.; Zia, M. F.; Wencel-Delord, J.; Besset, T.; Maes, B. U. W.; Schnürch, M. A Comprehensive Overview of Directing Groups Applied in Metal-Catalyzed C−H Functionalization Chemistry. *Chem. Soc. Rev.* **2018**, *47*, 6603−6743. (f) Dey, A.; Sinha, S. K.; Achar, T. K.; Maiti, D. Accessing Remote meta- and para-C(sp^2)−H Bonds with Covalently Attached Directing Groups. *Angew. Chem., Int. Ed.* **2019**, *58*, 10820−10843. (g) Rej, S.; Ano, Y.; Chatani, N. Bidentate Directing Groups: An Efficient Tool in C−H Bond Functionalization Chemistry for the Expedient Construction of C−C Bonds. *Chem. Rev.* **2020**, *120*, 1788−1887.

https://dx.doi.org/10.1021/acs.joc.0c02776
J. Org. Chem. XXXX, XXX, XXX−XXX

(6) Zhang, G.; Yu, H.; Qin, G.; Huang, H. Rh-Catalyzed Oxidative C−H Activation/Annulation: Converting Anilines to Indoles Using Molecular Oxygen as the Sole Oxidant. *Chem. Commun.* **2014**, *50*, 4331−4334.
(7) Kumar, G. S.; Kumar, P.; Kapur, M. Traceless Directing-Group Strategy in the Ru-Catalyzed, Formal [3 + 3] Annulation of Anilines with Allyl Alcohols: A One-Pot, Domino Approach for the Synthesis of Quinolines. *Org. Lett.* **2017**, *19*, 2494−2497.
(8) For recent reviews, see: (a) St John-Campbell, S.; Bull, J. A. Transition Imines as "Next Generation" Directing Groups for the Catalytic Functionalisation of C−H Bonds in a Single Operation. *Org. Biomol. Chem.* **2018**, *16*, 4582−4595. (b) Bhattacharya, T.; Pimparkar, S.; Maiti, D. Combining Transition Metals and Transient Directing Groups for C−H Functionalizations. *RSC Adv.* **2018**, *8*, 19456−19464. (c) Gandeepan, P.; Ackermann, L. Transient Directing Groups for Transformative C−H Activation by Synergestic Metal Catalysis. *Chem.* **2018**, *4*, 199−222. (d) Rej, S.; Chatani, N. Rhodium-Catalyzed $C(sp^2)$− or $C(sp^3)$−H Bond Functionalization Assisted by Removable Directing Groups. *Angew. Chem., Int. Ed.* **2019**, *58*, 8304−8329.
(9) For alkenes examples: (a) Liu, B.; Fan, Y.; Gao, Y.; Sun, C.; Xu, C.; Zhu, J. Rhodium(III)-Catalyzed N-Nitroso-Directed C−H Olefination of Arenes. High-Yield, Versatile Coupling under Mild Conditions. *J. Am. Chem. Soc.* **2013**, *135*, 468−473. (b) Yu, S.; Li, X. Rhodium(III)-Catalyzed C−C Coupling of Arenes with 2-Vinyloxiranes: Synthesis of Allylic Alcohols. *Org. Lett.* **2014**, *16*, 1200−1203. (c) Tian, M.; Yang, X.; Zhang, B.; Liu, B.; Li, X. Rh(III)-Catalyzed α-Fluoroalkenylation of N-Nitrosoanilines with 2,2-Difluorovinyl Tosylates via C−H Bond Activation. *Org. Chem. Front.* **2018**, *5*, 3406−3409. For alkynes examples: (d) Liu, B.; Song, C.; Sun, C.; Zhou, S.; Zhu, J. Rhodium(III)-Catalyzed Indole Synthesis Using N−N Bond as an Internal Oxidant. *J. Am. Chem. Soc.* **2013**, *135*, 16625−16631. (e) Wang, C.; Huang, Y. Traceless Directing Strategy: Efficient Synthesis of N-Alkyl Indoles via Redox-Neutral C−H Activation. *Org. Lett.* **2013**, *15*, 5294−5297. (f) Liang, Y.; Jiao, N. Cationic Cobalt(III) Catalyzed Indole Synthesis: The Regioselective Intermolecular Cyclization of N-Nitrosoanilines and Alkynes. *Angew. Chem., Int. Ed.* **2016**, *55*, 4035−4039. For other recent examples: (g) Hu, X.; Chen, X.; Shao, Y.; Xie, H.; Deng, Y.; Ke, Z.; Jiang, H.; Zeng, W. Co(III)-Catalyzed Coupling-Cyclization of Aryl C−H Bonds with α-Diazoketones Involving Wolff Rearrangement. *ACS Catal.* **2018**, *8*, 1308−1312. (h) Tan, G.; You, Q.; You, J. Iridium-Catalyzed Oxidative Heteroarylation of Arenes and Alkenes: Overcoming the Restriction to Specific Substrates. *ACS Catal.* **2018**, *8*, 8709−8714.
(10) (a) Nicolaou, K. C.; Mathison, C. J. N.; Montagnon, T. *o*-Iodoxybenzoic Acid (IBX) as a Viable Reagent in the Manipulation of Nitrogen- and Sulfur-Containing Substrates: Scope, Generality, and Mechanism of IBX-Mediated Amine Oxidations and Dithiane Deprotections. *J. Am. Chem. Soc.* **2004**, *126*, 5192−5201. (b) Potturi, H. K.; Gurung, R. K.; Hou, Y. Nitromethane with IBX/TBAF as a Nitrosating Agent: Synthesis of Nitrosamines from Secondary or Tertiary Amines under Mild Conditions. *J. Org. Chem.* **2012**, *77*, 626−631. (c) Zhadankin, V. V. Organoiodine (V) Reagents in Organic Synthesis. *J. Org. Chem.* **2011**, *76*, 1185−1197. For reviews, see: (d) Csende, F. Alkyl Nitrites as Valuable Reagents in Organic Synthesis. *Mini-Rev. Org. Chem.* **2015**, *12*, 127−148. (e) Li, P.; Jia, X. tert-Butyl Nitrite (TBN) as a Versatile Reagents in Organic Synthesis. *Synthesis* **2018**, *50*, 711−722.
(11) (a) Shank, R. C. Toxicology of N-Nitroso Compounds. *Toxicol. Appl. Pharmacol.* **1975**, *31*, 361−368. (b) Hecht, S. S. Biochemistry, Biology, and Carcinogenecity of Tobacco-Specific N-Nitrosoamines. *Chem. Res. Toxicol.* **1998**, *11*, 559−603. (c) *N-Nitrosoamines: 15 Listings*; National Toxicology Program, U.S. Department of Health and Human Services; November 2016, 14th Report on Carcinogens [online]; https://ntp.niehs.nih.gov/ntp/roc/content/profiles//nitrosamines.pdf (accessed Nov 23, 2020).
(12) Si, T.; Kim, H. Y.; Oh, K. Substrate Promiscuity of *ortho*-Naphthoquinone Catalyst: Catalytic Aerobic Amine Oxidation Protocols to Deaminative Cross-Coupling and N-Nitrosation. *ACS Catal.* **2019**, *9*, 9216−9221.
(13) For the detailed optimization of ***o*-NQ**-catalyzed aerobic *N*-nitrosation of *N*-methylaniline **1a**, please see the Supporting Information.
(14) *Q3C-Tables and List Guidance for Industry*; U.S. Department of Health and Human Services, Food and Drug Administration; June 2017; ICH, Revision 3.
(15) (a) D'Agostino, J. T.; Jaffe, H. H. Assignment of Electronic Transitions in the N-Alkyl-N-nitrosoanilines. *J. Am. Chem. Soc.* **1970**, *92* (17), 5160−5166. (b) Jaffe, H. H.; D'Agostino, J. T. Structural Studies on N-Alkyl-N-nitroanilines by Nuclear Magnetic Resonance. *J. Org. Chem.* **1971**, *36*, 992−995.
(16) Chaudhary, P.; Korde, R.; Gupta, S.; Sureshbabu, P.; Sabiah, S.; Kandasamy, J. An Efficient Metal-Free Method for the Denitrosation of Aryl N-Nitrosamines at Room Temperature. *Adv. Synth. Catal.* **2018**, *360*, 556−561.
(17) Our attempts to utilize the metal reduction protocols such as Fe/NH_4Cl, Zn/NH_4Cl, and $SnCl_2/HCl$ only led to the decomposition of the starting materials **5p**−**5t**. The denitrosation methods ($CuCl/HCl$, $NiCl_2/NaBH_4$, and $Fe(CO)_5$) utilized by the Zhu group in ref 9a also failed with **5p**−**5t**. The use of thiourea dioxide as reductant did not provide the desired denitrosated products: Chanuhary, P.; Gupta, S.; Sureshbabu, P.; Sabiah, S.; Kandasamy, J. A Metal Free Reduction of Aryl-N-nitrosamines to the Corresponding Hydrazines Using a Sustainable Reductant Thiourea Dioxide. *Green Chem.* **2016**, *18*, 6215−6221.
(18) The decomposition pathway of ***o*-NQ** catalyst through the cleavage of diketone carbon is speculated because the crude mixture did not have the typical carbonyl peaks in the IR and NMR analysis.
(19) The 2-nitropropane is converted to acetone after serving as the "NO" source in the ***o*-NQ**-catalyzed aerobic *N*-nitrosation; see ref 12 for details.
(20) The Rh(III)-catalyzed C−H activation reaction was not sensitive to the reaction concentrations in EtOH: **3a** in 91% (0.20 M), 92% (0.43 M), 89% (0.65 M), and 90% (1.30 M). However, the concentration beyond 2.6−3.6 M led to the formation of **3a** in 60−62% yields.
(21) Srivastava, S.; Ruane, P. H.; Toscano, J. P.; Sullivan, M. B.; Cramer, C. J.; Chiapperino, D.; Reed, E. C.; Falvey, D. E. Structures of Reactive Nitrenium Ions: Time-Resolved Infrared Laser Flash Photolysis and Computational Studies of Substituted N-Methyl-N-arylnitrenium Ions. *J. Am. Chem. Soc.* **2000**, *122*, 8271−8278.
(22) Jiao, J.; Zhang, X.; Chang, N.; Wang, J.; Wei, J.; Shi, X.; Chen, Z. A Facile and Practical Copper Powder-Catalyzed, Organic Solvent- and Ligand-Free Ullmann Amination of Aryl Halides. *J. Org. Chem.* **2011**, *76*, 1180−1183.
(23) Qiu, S.; Zhang, C.; Qiu, R.; Yin, G.; Huang, J. One-Pot Domino Synthesis of Diarylalkynes/1,4-Diaryl-1,3-diynes by [9,9-Dimethyl-4,5-bis(diphenylphosphino)xanthene] (Xantphos)-Copper(I) Iodide-Palladium(II) Acetate-Catalyzed Double Sonogashira-Type Reaction. *Adv. Synth. Catal.* **2018**, *360*, 313−321.
(24) Brown, A. E.; Eichler, B. E. Symmetric Diarylacetylenes: One-Pot Syntheses and Solution Photoluminescence. *Tetrahedron Lett.* **2011**, *52*, 1960−1963.
(25) Joshi, M.; Patel, M.; Tiwari, R.; Verma, A. K. Base-Mediated Selective Synthesis of Diversely Substituted N- Heterocyclic Enamines and Enaminones by the Hydroamination of Alkynes. *J. Org. Chem.* **2012**, *77*, 5633−5645.
(26) Zhou, S.; Wang, J.; Wang, L.; Chen, K.; Song, C.; Zhu, J. Co(III)-Catalyzed, Internal and Terminal Alkyne-Compatible Synthesis of Indoles. *Org. Lett.* **2016**, *18*, 3806−3809.
(27) Moon, Y.; Jeong, Y.; KooK, D.; Hong, S. Rh(III)-catalyzed Direct C−H/C−H Cross-Coupling of Quinones with Arenes Assisted by a Directing Group: Identification of Carbazole Quinones as GSKβ Inhibitors. *Org. Biomol. Chem.* **2015**, *13*, 3918−3923.
(28) Zhou, S.; Wang, J.; Zhang, F.; Song, C.; Zhu, J. A Versatile, Traceless C−H Activation-Based Approach for the Synthesis of Heterocycles. *Org. Lett.* **2016**, *18*, 2427−2430.

https://dx.doi.org/10.1021/acs.joc.0c02776
J. Org. Chem. XXXX, XXX, XXX−XXX