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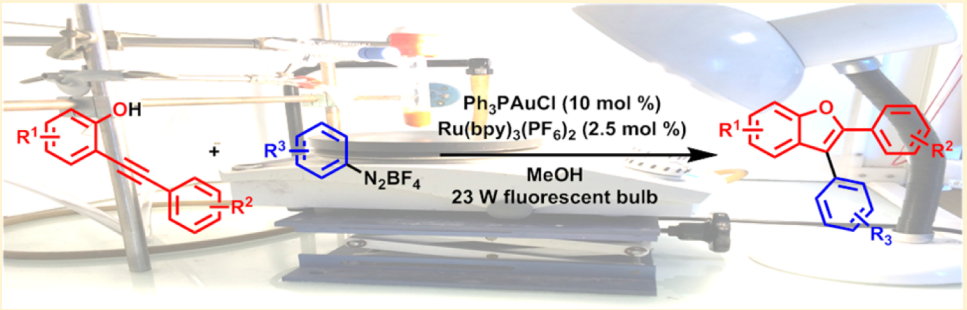
Dual Photoredox/Gold Catalysis Arylative Cyclization of *o*-Alkynylphenols with Aryldiazonium Salts: A Flexible Synthesis of Benzofurans

Zhonghua Xia, Omar Khaled, Virginie Mouriès-Mansuy, Cyril Ollivier,* and Louis Fensterbank*

Sorbonne Universités UPMC Univ Paris 06, CNRS, UMR 8232, Institut Parisien de Chimie Moléculaire, 4 place Jussieu, C.229, F-75005 Paris, France

Supporting Information



ABSTRACT: A new method for the arylative cyclization of *o*-alkynylphenols with aryldiazonium salts via dual photoredox/gold catalysis is described. The reaction proceeds smoothly at room temperature in the absence of base and/or additives and offers an efficient approach to benzofuran derivatives. The scope of the transformation is wide, and the limitations are discussed. The reaction is proposed to proceed through a photoredox-promoted generation of a vinylgold(III) intermediate that undergoes reductive elimination to provide the heterocyclic coupling adduct.

INTRODUCTION

Homogeneous gold catalysis has received a great deal of attention over the past decade. The majority of reports rely on the π-acidity of either gold(I) or gold(III) complexes to activate multiple bonds present on substrates such as alkenes, allenes, and, especially, alkynes toward nucleophilic attack.[1,2]

The selective activation of the carbon−carbon multiple bond by the gold complex generally constitutes the preliminary triggering event of the catalytic cycle.[3] Whereas a wide range of different intra- and intermolecular nucleophiles may be employed in these processes, in the vast majority of cases, the organogold species generated upon nucleophilic attack undergoes protodemetalation[4] leading to hydrofunctionalized products (Scheme 1a).

In some instances, the vinyl- or arylgold intermediate instead of undergoing protodemetalation can be advantageously trapped by an external electrophile such as a halide[5] or carbon dioxide.[6] Alternatively, cross coupling reaction with a nucleophilic partner in the presence of an external oxidant has been developed.[7] More recently, the groups of Glorius and Toste[8] reported a redox-neutral approach, avoiding the use of strong external oxidants, by merging gold and visible light photoredox catalysis[9] in a dual catalytic event.[10] In these transformations, the protodemetalation step can be rerouted in favor of an arylation step because of the presence of photoredox-generated aryl radicals. Presumably, Au(I) is oxidized in a stepwise fashion by the photogenerated aryl radical and the photocatalyst, leading to a cationic Au(III) species, which already bears the aryl coupling partner. Coordination of the π-system and nucleophilic attack then lead selectively to the cross coupling product. This proposed mechanism has recently been supported by DFT calculations[11] and the isolation of arylgold(III) complexes under related experimental conditions.[12] Extensions of this process to alkynylgold[13] and vinylgold[14] intermediates have also been explored (Scheme 1b).

Because of our interest in gold catalysis[15] and photoredox/organometallic dual catalysis reactions,[16] we herein report the successful development of a dual Au and photoredox catalytic system that can be applied to the intramolecular oxyarylation of alkynes with aryldiazonium salts (Scheme 1c). This process involves the formation of new C−Nu and C═C bonds across the alkyne and occurs at room temperature upon irradiation with a simple household light bulb. During the course of our investigations into these new dual catalytic events, two reports of alkyne difunctionalization by dual photoredox/gold catalysis appeared in the literature. The groups of Hashmi showed that under blue LED irradiation but in the absence of any photosensitizer, a gold-catalyzed intermolecular difunctionaliza-

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Scheme 1. Gold-Catalyzed Addition to C≡C Multiple Bonds

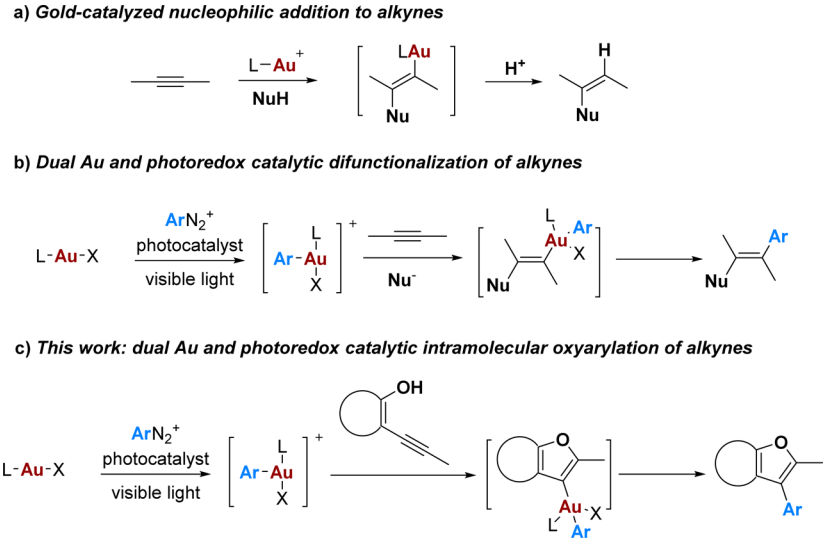
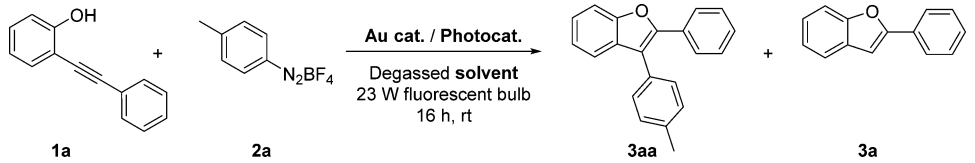


Table 1. Optimization of the Reaction Conditions[a]



1a 2a 3aa 3a

entry	Au catalyst	photocatalyst	solvent	yield of 3aa[b] (%)
1	$Ph_3PAuNTf_2$	$Ru(bpy)_3(PF_6)_2$	MeOH	<5 (3a, 60)
2	IPrAuCl	$Ru(bpy)_3(PF_6)_2$	MeOH	9 (3a, 35)
3	Ph_3PAuCl[d]	$Ru(bpy)_3(PF_6)_2$	MeOH	45 (3a, 40)
4	**Ph_3PAuCl**	**$Ru(bpy)_3(PF_6)_2$**	**MeOH**	**75 (73)**[c]
5[e]	Ph_3PAuCl	none	MeOH	<5 (3a, 30)
6[e]	Ph_3PAuCl	$Ru(bpy)_3(PF_6)_2$	MeOH	<5 (3a, 20)
7	Ph_3PAuCl	Eosin Y[e]	MeOH	8 (3a, 60)
8	–	$Cu(dpp)_2PF_6{\cdot}2H_2O$[d]	MeOH	<5; 3a not detected
9	Ph_3PAuCl	$Cu(dpp)_2PF_6{\cdot}2H_2O$[d]	MeOH	57
10	Ph_3PAuCl	$Ru(bpy)_3(PF_6)_2$	MeOH:MeCN (3:1)	60
11	Ph_3PAuCl	$Ru(bpy)_3(PF_6)_2$	MeOH:MeCN (4:1)	61
12	Ph_3PAuCl	$Ru(bpy)_3(PF_6)_2$	MeOH:MeCN (9:1)	66
13[f]	Ph_3PAuCl	$Ru(bpy)_3(PF_6)_2$	MeOH	48
14[g]	Ph_3PAuCl	$Ru(bpy)_3(PF_6)_2$	MeOH	39

[a]General conditions: **1a** (0.2 mmol), [Au] catalyst (10 mol %), photocatalyst (2.5 mol %), **2a** (0.8 mmol), degassed solvent (2 mL), rt, 16 h, 23 W fluorescent light bulb. [b]Determined by ^1H NMR using butadiene sulfone as an internal standard. [c]Isolated yield. [d]Concentration of 5 mol % used. [e]Reaction performed in the dark. [f]Three equivalents of **2a**. [g]Two equivalents of **2a**. IPr, 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene. dpp, 2,9-diphenyl-1,10-phenanthroline.

tion of alkynes with aryldiazonium salts delivering α-arylketones takes place smoothly.[14c] The group of Glorius focused on propargylic alcohols to develop an arylative version of the Meyer–Schuster rearrangement.[14d]

In this report, a single example of intramolecular reaction was given for *o*-alkynylphenol substrate **1a** and phenyldiazonium salt **2f**, coincidentally corresponding to one of our findings (benzofuran **3af**).[17−19] The full scope and limitations of this transformation are discussed here.

RESULTS AND DISCUSSION

Initial studies of the screening of various gold(I) catalysts revealed that the reaction of 2-(phenylethynyl)phenol **1a** with *p*-tolyldiazonium salt **2a** (4 equiv) in the presence of Ph_3PAuCl (10 mol %), $Ru(bpy)_3(PF_6)_2$ (5 mol %), and visible light in degassed MeOH (0.1 M) gave the best yield (73%) of product **3aa** (Table 1, entry 4). The cationic gold salt PPh_3AuNTf_2 or IPrAuCl did not give satisfactory results, and the product of classical cycloisomerization **3a** was obtained instead (Table 1, entries 1 and 2).[20] Interestingly, also, the presence of a photocatalyst or light proved to be necessary[14c] because the reaction with PPh_3AuCl alone afforded only traces of arylative cyclization (entries 5 and 6). On the basis of the involved redox potentials, the use of Eosin Y (E^*_{ox} = −1.6 V vs SCE)[21] and $Cu(dpp)_2PF_6{\cdot}2H_2O$ (E^*_{ox} = −1.11 V vs SCE)[22] (5 mol %) with or without PPh_3AuCl (entries 7−9) was tested, but it could not improve the yield. The use of mixed solvents was not helpful either (entries 10−12), and decreasing the number of

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equivalents of diazonium salt led to lower yields (entries 13 and 14).

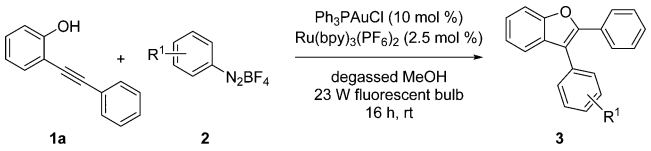
Next, the scope of aryldiazonium salts was studied in reactions with 2-(phenylethynyl)phenol **1a** under the optimal reaction conditions as described in entry 3 of Table 1. 3-(4-Nitrophenyl)-2-phenylbenzofuran **3ab** was obtained in 86% yield using *p*-nitroaryldiazonium salt as an arylation agent (Table 2). Aryldiazonium salts bearing other electron-withdrawing CF_3 (**2c**), CN (**2d**), and Br (**2e**) groups at the *para* position reacted smoothly with **1a**, delivering the corresponding arylated benzofurans **3ac**, **3ad**, and **3ae**, respectively, in good to excellent yields (entries 3−5). A good yield (65%) of 2,3-diphenylbenzofuran **3af**[17] (entry 6) could be obtained when phenyldiazonium salt was subjected to the reaction, but an electron-donating OCH_3 group led to a lower yield of coupling product **3ag** (23%). An aryldiazonium salt containing an ester group at the *meta* position was also tolerated well (**3ah**). However, a substituent at the *ortho* position of the aryldiazonium salt had a dramatic effect on this arylative cyclization reaction and resulted in a much lower yield (compare **3ad**, entry 4, vs **3ai**, entry 9).

The effect of substitution on both aromatic rings of *o*-alkynylphenols **1** was then investigated in reactions with aryldiazonium salts (Table 3). *o*-Alkynylphenol **1j** bearing an electron-donating methoxy group in the *para* position to the alkyne gave a sluggish reaction. Expected coupling product **3jd** was isolated in only 6% yield. The major isolated product was the known[23] ester **4** (21%), resulting presumably from a preferential gold-catalyzed hydromethoxylation of the alkyne moiety [involving intermediate **E** (Scheme 4)], followed by a gold-catalyzed oxidative cleavage of the generated enol ether.[24] In sharp contrast, precursors with an electron-withdrawing ester group at the *para* or *meta* position, when reacted with 4-cyanophenyldiazonium salt, delivered the corresponding arylated benzofurans in good yields (**3kd** and **3ld**).

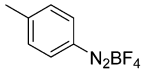
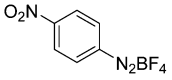
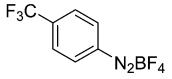
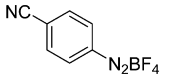
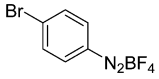
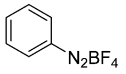
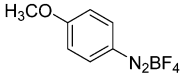
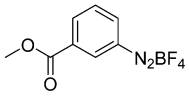
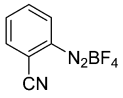
o-Alkynylphenol bearing a *p*-tolyl group attached to the alkyne reacted efficiently with *p*-nitrophenyldiazonium tetrafluoroborate and afforded the corresponding 3-(4-nitrophenyl)-2-(*p*-tolyl)benzofuran **3mb** in 85% yield (Scheme 2). Here also, the expected reaction was diverted when an electron donor (OMe) was present as on 2-[(4-methoxyphenyl)ethynyl]-phenol **1n**. In that case, unarylated 2-phenylbenzofuran **3n** was isolated in 96% yield, suggesting that the vinylgold intermediate undergoes competitive protodeauration. Similarly, *p*-cyanoaryldiazonium salt **3n** was formed in 48% yield accompanied by an 11% yield of arylative cyclization product **3nd**.

The use of CF_3-alkynylphenol **1o** provided another series of contrasting results (Scheme 3). Arylation took place with phenyldiazonium salt **2f**, but there was no formation of the benzofuran moiety. Instead, an α,α'-bis-arylated ketone bearing a phenol moiety was isolated in good yield (77%). On the basis of the fact that no cyclization of the phenol took place but that the vinylgold intermediate was presumably trapped by methanol in the β position to gold,[14c,d] we proposed regioisomeric ketone structure of **5of** (originating from the hydrolysis of the enol ether intermediate). The same type of reactivity was observed with 4-nitrophenyldiazonium salt **2b**, giving in that case the *E*/*Z* mixture of the more stable arylated

Table 2. Scope of Aryldiazonium Salts[a]

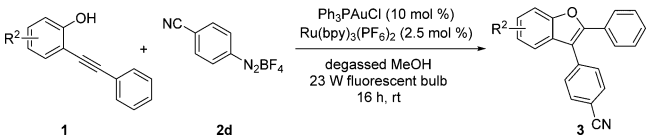


1a 2 3

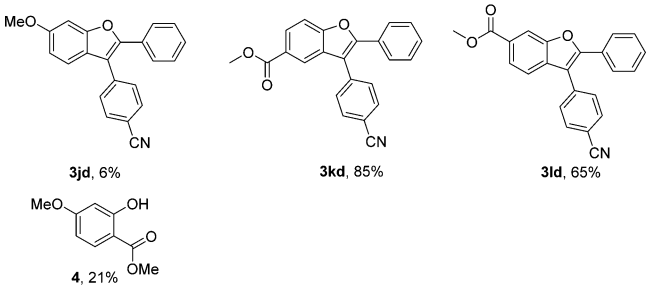
entry	2		3, yield(%)
1		**2a**	**3aa**, 73%
2		**2b**	**3ab**, 86%
3		**2c**	**3ac**, 76%
4		**2d**	**3ad**, 81%
5		**2e**	**3ae**, 61%
6		**2f**	**3af**, 65%
7		**2g**	**3ag**, 23%
8		**2h**	**3ah**, 62%
9		**2i**	**3ai**, 37%

[a]Reaction conditions: **1a** (0.2 mmol) and **2** (4 equiv), Ph_3PAuCl (10 mol %), $Ru(bpy)_3(PF_6)_2$ (2.5 mol %), degassed methanol (2 mL) under Ar, rt, 16 h, 23 W fluorescent light bulb. Isolated yields of **3** are listed.

Table 3. Influence of a Substituent on the Phenol Moiety of *o*-Alkynylphenols



1 2d 3



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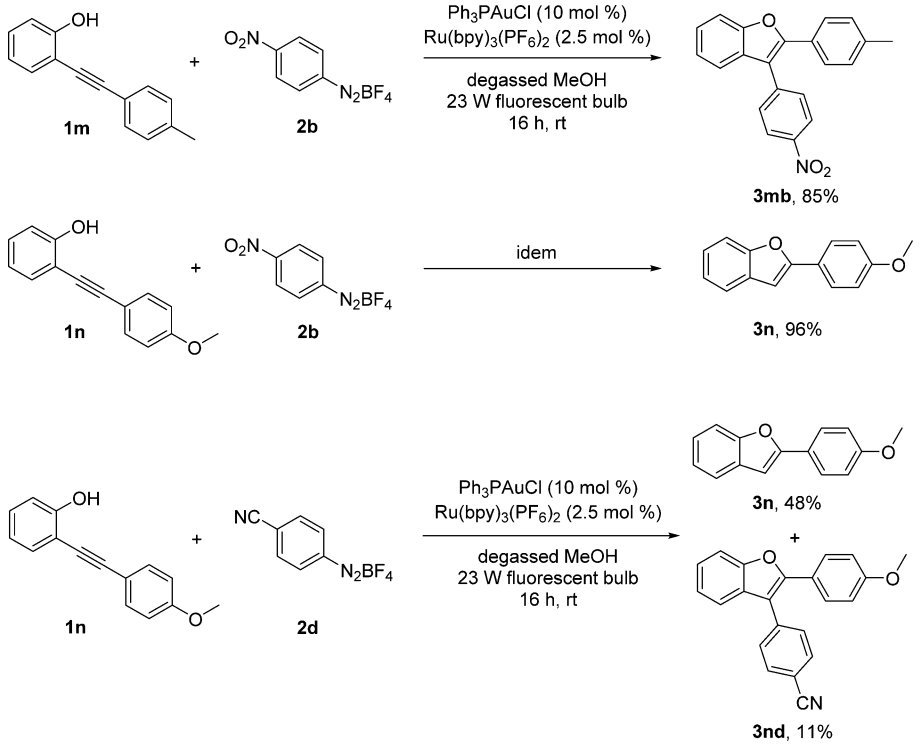
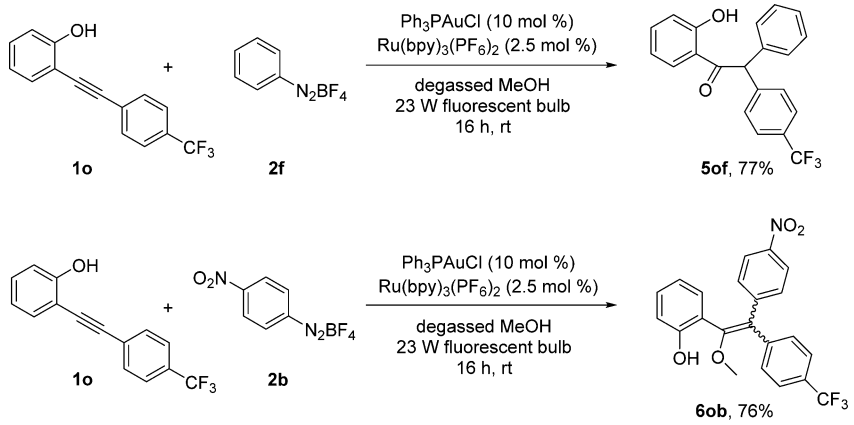
Scheme 2. Influence of an Electron-Donating Substituent on the Acetylene Moiety of *o*-Alkynylphenols



Scheme 3. Influence of an Electron-Withdrawing Substituent on the Acetylene Moiety of *o*-Alkynylphenols



enolethers **6ob** (76%). All these findings suggest important electronic effects influencing the regioselectivity of the arylation step that we rationalize below. Finally, we also examined the reactivity of butyl-substituted and terminal *o*-alkynylphenols under the same dual catalysis conditions. Unfortunately, complex reaction mixtures were obtained in both cases when using aryldiazonium salt **2d** as the radical source.[25]

On the basis of previous studies of dual Au/photoredox catalysis, a mechanism involving a photoredox-induced homogeneous Au(I)/Au(III) redox cycle was proposed (Scheme 4). Upon irradiation with visible light, the reaction of ArN_2BF_4 **2** with photoexcited $Ru(bpy)_3^{2+*}$ generates $Ru(bpy)_3^{3+}$ and an aryl radical that reacts with the gold(I) catalyst to initially generate gold(II)−aryl complex **A**. This gold(II) intermediate is further oxidized by Ru^{III}, giving gold(III)−aryl complex **B** and regenerating the photocatalyst. The 5-*endo-dig* cyclization by intramolecular nucleophilic attack on complex **C** furnishes alkyne-derived heteroaryl−vinylgold-(III) intermediates **D**, which undergo reductive elimination to give desired product **3** and regenerate the gold(I) catalyst. When R^2 is an electron donor (methoxy in the *para* position), the basicity of the corresponding vinylgold intermediate **D** would significantly increase,[4b] rendering the protodeauration highly competitive. This would divert the catalytic cycle to the simple cycloisomerization process to give products **3a** and **3n**. In the case in which R^2 bears an electron-withdrawing moiety (4-CF_3 phenyl group), slippage of gold metal[26] would yield to vinylgold complex **E** as the preferred intermediate. The latter cannot be intramolecularly intercepted by the phenol moiety, so methanol adds intermolecularly to give a mixture of enol ethers that would be isolated (**6ob**, *E*:*Z*, 1:1) or hydrolyzed (ketone **5of**). Reductive elimination would still take place to give arylation and propagate the catalytic cycle.

In summary, we have developed a novel photoredox/gold dual catalysis process that could be applied to the preparation of various benzofuran derivatives by arylative cyclization of *o*-

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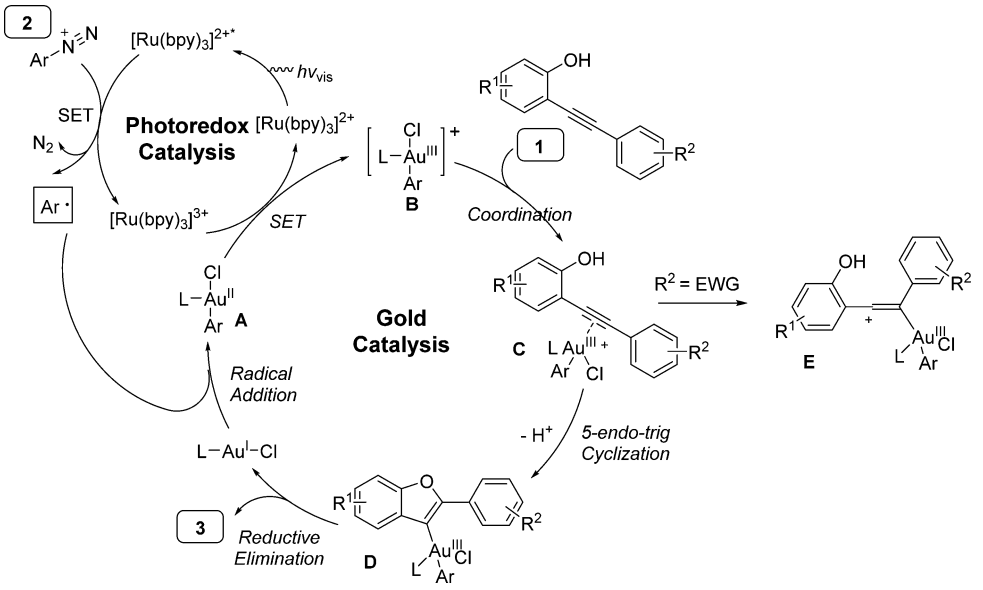
Scheme 4. Proposed Reaction Mechanisms



alkynylphenols with aryldiazonium salts. The reaction takes place smoothly at room temperature in the absence of additives, providing good to excellent yields of heterocyclic scaffolds. It presumably involves a vinylgold(III) intermediate that is generated through two concurrent catalytic cycles. The electronic demand of the aryl substituent exerts an important influence on the efficiency and regioselectivity of the arylation step.

This work constitutes one more example of a successful dual catalytic approach relying in part on an efficient photoredox-catalyzed event and augurs well for further exciting developments in this domain.

EXPERIMENTAL SECTION

General Experimental Details. All reactions involving air sensitive reagents or intermediates were conducted in preheated glassware under an atmosphere of dry argon using standard Schlenk techniques. Reagents and chemicals were purchased from commercial sources and used as received. Methanol and acetonitrile were purified by means of distillation under a dry argon atmosphere on calcium hydride. The reaction mixtures were irradiated by a standard household lamp with a 23 W fluorescent light bulb. Aryldiazonium tetrafluoroborates **2a**–**2i** were synthesized following the procedure of Hanson.[27] Photocatalysts $[Ru(bpy)_3]_2(PF_6)_2$ (bpy = 2,2′-bipyridine) and $Cu(dpp)_2PF_6{\cdot}2H_2O$ (dpp = 2,9-diphenyl-1,10-phenanthroline) were prepared according to the procedures of Yoon[28] and Meyer,[29] respectively. The gold(I) complexes $Ph_3PAuNTf_2$ and IPrAuCl [IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene] were purchased from commercial suppliers. Chromatographic purification was performed over silica gel (LC60A) SI 60 Å (40–63 μm). Thin layer chromatography (TLC) was performed with silica gel 60 F_{254} precoated on aluminum plates and visualized by UV light and/or staining with $KMnO_4$. Infrared (IR) spectra were recorded on an ATR spectrophotometer, and only the strongest or structurally most important peaks were listed. Melting points were determined in open capillary tubes and are uncorrected. ^1H, ^{19}F, and ^{13}C NMR spectra were recorded at room temperature at 400, 377, and 100 MHz, respectively, or at 300, 282, and 75 MHz, respectively. Chemical shifts (δ) are reported in parts per million, and coupling constants (J) are given in hertz. The following abbreviations were used for peak multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; quat, quaternary; quint, quintet; sept, septet; m, multiplet; br, broad. Values were referenced relative to residual $CDCl_3$ proton signals at δ 7.26 and 77.16 for ^{13}C NMR and referenced relative to residual $CFCl_3$ at δ 0.00 for ^{19}F. High-resolution mass spectrometries were performed on an LTQ Orbitrap instrument (ESI) and on a microTOF instrument (ESI).

General Procedure 1 (GP1). *Synthesis of 2-(Phenylethynyl)-phenol* ***1a****.*[30] MOMCl (1.1 g, 13.6 mmol, 1.5 equiv) was added to a mixture of 2-iodophenol (2 g, 9.1 mmol, 1 equiv) and K_2CO_3 (5.0 g, 36.36 mmol, 4 equiv) in DMF (8 mL). The mixture was stirred at room temperature for 2 h. The completion of the reaction was monitored by TLC (9:1 Pent:Et_2O). The solution was diluted with diethyl ether (100 mL), and 60 mL of water was added. The layers were separated, and the aqueous phase was extracted with diethyl ether (3 × 30 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford the MOM iodide (2.4 g, quant). The latter was engaged without purification in the Sonogashira process. To a solution of phenylacetylene (1.0 g, 10.0 mmol, 1.1 equiv) and the MOM iodide (2.4 g, 9.1 mmol, 1.0 equiv) in triethylamine (90 mL) were added $PdCl_2(PPh_3)_2$ (126.3 mg, 0.18 mmol, 2 mol %) and CuI (34.3 mg, 0.18 mmol, 2 mol %). The mixture was stirred at 65 °C until complete consumption of MOM iodide was observed by TLC (9:1 Pent:Et_2O). The reaction mixture was warmed to room temperature; diethyl ether was added (50 mL), and the mixture was filtered through a plug of cotton wool. After removal of the solvent, the residue was purified by silica gel chromatography (9:1 Pent:Et_2O) to afford the MOM 2-(phenylethynyl)phenol (1.95 g, 91%). The deprotection of MOM was conducted by adding HCl (0.85 mL, 9.0 mmol, 6 N) to a solution of the previous compound (1.95 g, 8.2 mmol) in MeOH (15 mL). The reaction mixture was stirred until the deprotection was completed. The mixture was diluted with water (50 mL) and diethyl ether (30 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (3 × 30 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford 2-(phenylethynyl)phenol as a yellow solid (1.3 g, 82%) after purification by flash chromatography (9:1 Pent:Et_2O).

General Procedure 2 (GP2). *Arylative Cyclization of o-Alkynylphenols with Aryldiazonium Salts.* The photocatalyst $[Ru(bpy)_3](PF_6)_2$ (4.3 mg, 0.005 mmol, 2.5 mol %), the gold(I) complex Ph_3PAuCl (9.9 mg, 0.02 mmol, 10 mol %), the appropriate diazonium salt **2** (0.8 mmol), and *o*-alkynylphenol derivative **1** (0.2 mmol) were introduced in a Schlenk tube equipped with a magnetic stirring bar to which MeOH (2 mL) had been added. The mixture was degassed using three freeze pump–thaw cycles and then irradiated with a 23 W fluorescent light bulb (~10 cm from the glassware; if necessary, the air

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flow can be used to cool the Schlenk tube) for 16 h (unless mentioned). The reaction was quenched with water (2 mL) and a saturated aqueous K_2CO_3 solution (1 mL), and the solution was extracted with Et_2O (4 × 5 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product. The residue was purified by FC on silica gel to afford the desired product.

Synthesis of *o*-Alkynylphenol Derivatives as Substrates. All *o*-alkynylphenol substrates were prepared according to the procedure reported by Hashmi et al.[30] and based on the synthesis of 2-(phenylethynyl)phenol **1a**, as summarized before in General Procedure 1 (GP1).

*2-(Phenylethynyl)phenol (**1a**).* Following general procedure GP1 with 2-iodophenol (2 g, 9.1 mmol) and phenylacetylene (1.0 g, 9.1 mmol) to afford **1a** (1.3 g, 74% over three steps). The spectroscopic data match those previously reported in the literature:[30] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60−7.56 (m, 2H), 7.46 (dd, J = 7.8, 1.8 Hz, 1H), 7.43−7.39 (m, 3H), 7.33−7.27 (m, 1H), 7.02 (dd, J = 8.1, 0.9 Hz, 1H), 6.94 (td, J = 7.5, 1.2 Hz, 1H), 5.87 (s, 1H).

*5-Methoxy-2-(phenylethynyl)phenol (**1j**).* Following general procedure reported by Frontier et al.[31] with 2-iodo-5-methoxyphenol and phenylacetylene. The spectroscopic data match those previously reported in the literature:[32] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54−7.51 (m, 2H), 7.32−7.27 (m, 4H), 6.56 (d, J = 2.4 Hz, 1H), 6.50 (dd, J = 6.3, 2.4 Hz, 1H), 5.87 (bs, 1H), 3.81 (s, 3H).

*Methyl 4-Hydroxy-3-(phenylethynyl)benzoate (**1k**).* Following general procedure GP1 with methyl 4-hydroxy-3-iodobenzoate (556 mg, 2 mmol) and phenylacetylene (224.7 mg, 2.2 mmol) to afford **1k** (413.7 mg, 82% over three steps). The spectroscopic data match those previously reported in the literature:[33] ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (d, J = 2.1 Hz, 1H), 7.96 (dd, J = 8.7, 2.1 Hz, 1H), 7.57−7.53 (m, 2H), 7.41−7.38 (m, 3H), 7.02 (d, J = 8.7 Hz, 1H), 6.26 (s, 1H), 3.90 (s, 3H).

*Methyl 3-Hydroxy-4-(phenylethynyl)benzoate (**1l**).* Following general procedure GP1 with methyl 3-hydroxy-4-iodobenzoate (556 mg, 2 mmol) and phenylacetylene (224.7 mg, 2.2 mmol) to afford **1l** (454 mg, 90% over three steps): mp 204−206 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (d, J = 1.5 Hz, 1H), 7.61−7.54 (m, 3H), 7.43 (d, J = 8.1 Hz, 1H), 7.40−7.38 (m, 3H), 5.95 (s, 1H), 3.92 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.3, 156.3, 131.7, 131.7, 131.6, 129.3, 128.6, 121.9, 121.5, 115.8, 114.3, 98.7, 82.5, 52.3; IR (neat) 3407, 2961, 2922, 2853, 1711, 1607, 1573, 1428, 1292, 1244, 1201, 1094, 986, 915, 881, 799, 755, 692, 590 cm^{-1}; HRMS calcd for $[C_{16}H_{12}NaO_3]^+$ 275.0684, found 275.0679.

*2-(p-Tolylethynyl)phenol (**1m**).* Following general procedure GP1 with 2-iodophenol (440 mg, 2 mmol) and 4-ethynyltoluene (255 mg, 2.2 mmol) to afford **1m** (292 mg, 70% over three steps). The spectroscopic data match those previously reported in the literature:[34] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46−7.40 (m, 3H), 7.30−7.24 (m, 1H), 7.20−7.17 (m, 2H), 6.99 (bdd, J = 8.4, 1.2 Hz, 1H), 6.91 (td, J = 7.5, 1.2 Hz, 1H), 5.85 (s, 1H), 2.39 (s, 3H).

*2-[(4-Methoxyphenyl)ethynyl]phenol (**1n**).* Following general procedure GP1 with 2-iodophenol (440 mg, 2 mmol) and 4-ethynylanisole (291 mg, 2.2 mmol) to afford **1n** (292 mg, 65% over three steps). The spectroscopic data match those previously reported in the literature:[35] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82−7.79 (m, 2H), 7.58−7.50 (m, 2H), 7.26−7.20 (m, 2H), 7.00−6.97 (m, 2H), 6.89 (s, 1H), 3.87 (s, 3H).

*2-{[4-(Trifluoromethyl)phenyl]ethynyl}phenol (**1o**).* Following general procedure GP1 with 2-iodophenol (440 mg, 2 mmol) and 4-(trifluoromethyl)phenylacetylene (374 mg, 2.2 mmol) to afford **1o** (424 mg, 81% over three steps). The spectroscopic data match those previously reported in the literature:[36] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (m, 4H), 7.44 (dd, J = 7.8, 1.5 Hz, 1H), 7.31 (bs, 1H), 7.00 (bd, J = 8.1 Hz, 1H), 6.94 (bt, J = 7.5 Hz, 1H), 5.76 (s, 1H).

Products of Arylative Cyclization of *o*-Alkynylphenols. *2-Phenylbenzofuran (**3a**).* The spectroscopic data match those previously reported in the literature:[37] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (dd, J = 8.4, 1.5 Hz, 2H), 7.59 (dd, J = 7.8, 1.8 Hz, 1H), 7.54 (d, J = 8.4 Hz, 1H), 7.46 (t, J = 7.5 Hz, 2H), 7.32−7−21 (m, 3H), 7.03 (s, 1H).

*2-Phenyl-3-(p-tolyl)benzofuran (**3aa**).* Following general procedure GP2 with *o*-alkynylphenol **1a** (38.8 mg, 0.2 mmol) and aryldiazonium **2a** (165 mg, 0.8 mmol). The crude product was purified by flash column chromatography (100:1 Pent:Et_2O) to afford **3aa** as a yellow solid (42 mg, 73%). The spectroscopic data match those previously reported in the literature:[38] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68−7.65 (m, 2H), 7.55−47 (m, 2H), 7.36 (dd, J = 6.0, 1.8 Hz, 2H), 7.34−7.19 (m, 7H), 2.43 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.0, 150.3, 137.3, 130.8, 130.4, 129.7, 129.7, 129.6, 128.4, 128.2, 127.0, 124.6, 122.8, 120.1, 117.5, 111.1, 21.4.

*3-(4-Nitrophenyl)-2-phenylbenzofuran (**3ab**).* Following general procedure GP2 with *o*-alkynylphenol **1a** (38.8 mg, 0.2 mmol) and aryldiazonium **2b** (190 mg, 0.8 mmol). The crude product was purified by flash column chromatography (100:1 Pent:Et_2O) to afford **3ab** as a yellow solid (54 mg, 86%). The spectroscopic data match those previously reported in the literature:[38] ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26 (d, J = 8.7 Hz, 2H), 7.70 (d, J = 8.7 Hz, 2H), 7.63−7.59 (m, 3H), 7.53−7.50 (m, 1H), 7.47−7.36 (m, 4H), 7.33−7.27 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.1, 151,9, 147.1, 140.2, 130.4, 129.8, 129.1, 128.9, 128.7, 127.4, 125.2, 124.2, 123.4, 119.4, 115.4, 111.4.

*2-Phenyl-3-[4-(trifluoromethyl)phenyl]benzofuran (**3ac**).* Following general procedure GP2 with *o*-alkynylphenol **1a** (38.8 mg, 0.2 mmol) and aryldiazonium **2c** (208 mg, 0.8 mmol). The crude product was purified by flash column chromatography (100:0 Pent:Et_2O) to afford **3ac** as a white solid (51 mg, 76%). The spectroscopic data match those previously reported in the literature:[39] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78−7.72 (m, 2H), 7.65−7.57 (m, 4H), 7.49 (d, J = 7.5 Hz, 1H), 7.39−7.26 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.1, 151.3, 136.9, 130.2, 130.1, 129.6, 128.8, 128.7, 128.6, 128.5, 127.2, 125.9 (q, J_{C-F} = 4.0 Hz), 125.0, 124.9, 124.2 (q, J_{CF^3} = 270.7 Hz), 123.3, 122.9, 120.9, 119.7, 116.1, 111.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ −62.43.

*4-(2-Phenylbenzofuran-3-yl)benzonitrile (**3ad**).* Following general procedure GP2 with *o*-alkynylphenol **1a** (38.8 mg, 0.2 mmol) and aryldiazonium **2d** (174 mg, 0.8 mmol). The crude product was purified by flash column chromatography (100:1 Pent:Et_2O) to afford **3ad** as a colorless solid (48 mg, 81%). The spectroscopic data match those previously reported in the literature:[40] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, J = 8.1 Hz, 2H), 7.75−7.57 (m, 4H), 7.50 (dt, J = 7.5, 1.2, 0.6 Hz, 1H), 7.41−7.34 (m, 4H), 7.31−7.26 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.2, 151.7, 138.2, 132.8, 130.4, 129.9, 129.1, 128.7, 127.4, 125.2, 123.4, 119.5, 118.8, 115.8, 111.4, 111.3.

*3-(4-Bromophenyl)-2-phenylbenzofuran (**3ae**).* Following general procedure GP2 with *o*-alkynylphenol **1a** (38.8 mg, 0.2 mmol) and aryldiazonium **2e** (217 mg, 0.8 mmol). The crude product was purified by flash column chromatography (100:0 Pent:Et_2O) to afford **3ae** as a white solid (43 mg, 61%): mp 120−122 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67−7.55 (m, 5H), 7.48 (dd, J = 7.5, 1.2 Hz, 1H), 7.41−7.23 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.0, 150.8, 132.2, 131.9, 131.4, 130.4, 129.8, 128.6, 128.5, 127.1, 124.9, 123.1, 121.7, 119.7, 116.3, 111.2; IR (neat) 2363, 2328, 1487, 1445, 1380, 1256, 1206, 1064, 1001, 956, 839, 804, 741, 681, 606 cm^{-1}; MS (EI, 70 eV) m/z 350 [**3ae** (^{81}Br)], 348 [**3ae** (^{79}Br)], 270 (**3ae** − Br + H).

*2,3-Diphenylbenzofuran (**3af**).* Following general procedure GP2 with *o*-alkynylphenol **1a** (38.8 mg, 0.2 mmol) and aryldiazonium **2f** (154 mg, 0.8 mmol). The crude product was purified by flash column chromatography (100:0 Pent:Et_2O) to afford **3af** as a colorless oil (35 mg, 65%). The spectroscopic data match those previously reported in the literature:[39] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (dd, J = 7.2, 2.7 Hz, 2H), 7.57 (d, J = 7.8 Hz, 1H), 7.51−7.42 (m, 6H), 7.35−7.22 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.0, 150.5, 132.9, 130.7, 130.3, 129.8, 129.0, 128.4, 128.3, 127.6, 127.0, 124.7, 122.9, 120.0, 117.5, 111.1.

*3-(4-Methoxyphenyl)-2-phenylbenzofuran (**3ag**).* Following general procedure GP2 with *o*-alkynylphenol **1a** (38.8 mg, 0.2 mmol) and aryldiazonium **2g** (178 mg, 0.8 mmol). The crude product was purified by flash column chromatography (100:0 Pent:Et_2O) to afford **3ag** as a white solid (14 mg, 23%). The spectroscopic data match those

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previously reported in the literature:[38] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (dd, J = 8.1, 2.1 Hz, 2H), 7.56 (d, J = 8.1 Hz, 1H), 7.51−7.48 (m, 1H), 7.44 (d, J = 8.7 Hz, 2H), 7.33−7.24 (m, 5H), 7.02 (d, J = 8.4 Hz, 2H), 3.89 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 154.0, 150.8, 130.9, 130.8, 130.5, 128.4, 128.2, 126.9, 124.9, 124.6, 122.8, 120.0, 117.1, 114.5, 111.1, 55.3.

*3-(2-Phenylbenzofuran-3-yl)benzoate (**3ah**).* Following general procedure GP2 with *o*-alkynylphenol **1a** (38.8 mg, 0.2 mmol) and aryldiazonium **2h** (200 mg, 0.8 mmol). The crude product was purified by flash column chromatography (100:1 Pent:Et_2O) to afford **3ah** as a colorless oil (41 mg, 62%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.23−8.22 (m, 1H), 8.11−8.08 (m, 1H), 7.69−7.46 (m, 6H), 7.38−7.28 (m, 4H), 7.26−7.23 (m, 1H), 3.93 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.8, 154.0, 150.9, 134.4, 133.3, 131.0, 130.8, 130.3, 129.9, 129.1, 128.8, 128.6, 128.5, 127.0, 124.9, 123.1, 119.8, 116.5, 111.2, 52.2; IR (neat) 2963, 2923, 2854, 1726, 1453, 1376, 1295, 1261, 1195, 1112, 1073, 750, 634 cm^{-1}; HRMS calcd for $[C_{22}H_{16}NaO_3]^+$ 351.0997, found 351.0992.

*2-(2-Phenylbenzofuran-3-yl)benzonitrile (**3ai**).* Following general procedure GP2 with *o*-alkynylphenol **1a** (38.8 mg, 0.2 mmol) and aryldiazonium **2i** (174 mg, 0.8 mmol). The crude product was purified by flash column chromatography (100:1 Pent:Et_2O) to afford **3ai** as a yellow oil (22 mg, 37%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (dd, J = 7.2, 1.5 Hz, 1H), 7.72 (td, J = 7.5, 1.5 Hz, 1H), 7.63−7.52 (m, 4H), 7.40−7.24 (m, 7H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.0, 152.2, 137.0, 133.9, 133.2, 131.6, 130.1, 129.5, 128.9, 128.7, 128.4, 126.8, 125.1, 125.1, 123.3, 119.6, 117.6, 113.8, 111.4; IR (neat) 2963, 2922, 2854, 1455, 1374, 1258, 1204, 1108, 754, 692 cm^{-1}; HRMS calcd for $[C_{21}H_{13}NNaO]^+$ 318.0895, found 318.0889.

*6-Methoxy-3-(4-methylphenyl)-2-phenylbenzofuran (**3jd**).* Following general procedure GP2 with *o*-alkynylphenol **1j** (37.6 mg, 0.17 mmol) and aryldiazonium **2d** (173 mg, 0.8 mmol). A mixture of products **4** and **3jd** was obtained and purified by flash column chromatography (100:6 Pent:Et_2O) to afford **4** as a colorless oil (6.4 mg, 21%) and **3jd** as a colorless oil in the presence of a trace of **4** (3 mg, 6%). Compound **4** is commercially available, and its spectroscopic data match those previously reported in the literature. Compound **4**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.0 (s, 1H), 7.73 (dd, J = 8.0, 0.4 Hz, 1H), 6.45−6.42 (m, 2H), 3.91 (s, 3H), 3.82 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4, 165.6, 163.8, 131.2, 107.6, 105.4, 100.7, 55.5, 51.9. Compound **3jd**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.8 Hz, 2H), 7.62 (d, J = 8.4 Hz, 2H), 7.57−7.54 (m, 2H), 7.36−7.33 (m, 4H), 7.11 (d, J = 2.0 Hz, 1H), 6.91 (dd, J = 8.4, 2.0 Hz, 1H), 3.90 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.7, 155.2, 150.7, 138.3, 132.7, 130.3, 130.1, 128.7, 128.7, 127.0, 122.5, 119.7, 118.8, 115.7, 112.4, 111.2, 95.9, 55.8; IR (neat) 3735, 3629, 2916, 2843, 2364, 2328, 2227, 1669, 1617, 1494, 1440, 1347, 1271, 1196, 1153, 1114, 1068, 1026, 971, 877, 833, 769, 695, 640, 586 cm^{-1}; HRMS calcd for $[C_{22}H_{15}NNaO_2]^+$ 348.0995, found 348.0983.

*Methyl 3-(4-Cyanophenyl)-2-phenylbenzofuran-5-carboxylate (**3kd**).* Following general procedure GP2 with *o*-alkynylphenol **1k** (50 mg, 0.2 mmol) and aryldiazonium **2d** (174 mg, 0.8 mmol). The crude product was purified by flash column chromatography (100:4 Pent:Et_2O) to afford **3kd** as a white solid (60 mg, 85%): mp 215−217 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.19 (dd, J = 1.8, 0.6 Hz, 1H), 8.10 (dd, J = 8.4, 1.5 Hz, 1H), 7.79−7.76 (m, 2H), 7.64−7.58 (m, 5H), 7.38−7.36 (m, 3H), 3.93 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.9, 156.6, 153.0, 137.3, 132.9, 130.4, 129.5, 129.3, 129.2, 128.8, 127.4, 126.9, 125.8, 121.9, 118.6, 116.0, 111.7, 111.3, 52.2; IR (neat) 2923, 2853, 2228, 1718, 1606, 1437, 1372, 1293, 1242, 1200, 1098, 991, 918, 848, 763, 692 cm^{-1}; HRMS calcd for $[C_{23}H_{15}NNaO_3]^+$ 376.0950, found 376.0944.

*Methyl 3-(4-Cyanophenyl)-2-phenylbenzofuran-6-carboxylate (**3ld**).* Following general procedure GP2 with *o*-alkynylphenol **1l** (50 mg, 0.2 mmol) and aryldiazonium **2d** (174 mg, 0.8 mmol). The crude product was purified by flash column chromatography (100:4 Pent:Et_2O) to afford **3ld** as a white solid (46 mg, 65%): mp 148−150 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26 (dd, J = 1.2, 0.6 Hz, 1H), 7.99 (dd, J = 6.9, 1.5 Hz, 1H), 7.78−7.75 (m, 2H), 7.63−7.58 (m, 4H), 7.50 (dd, J = 8.1, 0.6 Hz, 1H), 7.39−7.36 (m, 3H), 3.97 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.9, 154.5, 153.5, 137.4, 133.2, 132.9, 130.4, 129.7, 129.3, 128.8, 127.5, 127.0, 124.8, 119.0, 118.6, 115.8, 113.0, 111.7, 52.3; IR (neat) 2952, 2366, 2228, 1705, 1613, 1496, 1428, 1367, 1287, 1222, 1192, 1072, 974, 909, 869, 833, 760, 731, 686, 626 cm^{-1}; HRMS calcd for $[C_{23}H_{15}NNaO_3]^+$ 376.0950, found 376.0944.

*3-(4-Nitrophenyl)-2-(p-tolyl)benzofuran (**3mb**).* Following general procedure GP2 with *o*-alkynylphenol **1m** (42 mg, 0.2 mmol) and aryldiazonium **2b** (189 mg, 0.8 mmol). The crude product was purified by flash column chromatography (100:1 Pent:Et_2O) to afford **3mb** as a yellow oil (56 mg, 85%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.31 (d, J = 8.7 Hz, 2H), 7.69 (dd, J = 6.9, 1.8 Hz, 2H), 7.58 (d, J = 8.1 Hz, 1H), 7.52−7.48 (m, 3H), 7.39−7.34 (m, 1H), 7.31−7.26 (m, 1H), 7.17 (d, J = 8.1 Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.1, 152.3, 147.0, 140.4, 139.4, 130.4, 129.4, 129.0, 127.4, 126.9, 125.0, 124.2, 123.4, 119.3, 114.8, 111.4, 21.4; IR (neat) 2364, 2329, 1603, 1515, 1456, 1347, 1257, 1071, 859, 822, 750, 654, 610 cm^{-1}; HRMS calcd for $[C_{21}H_{15}NNaO_3]^+$ 352.0944, found 352.0945.

*2-(4-Methoxyphenyl)benzofuran (**3n**).* Following general procedure GP2 with *o*-alkynylphenol **1n** (45 mg, 0.2 mmol) and aryldiazonium **2b** (189 mg, 0.8 mmol). The crude product was purified by flash column chromatography (100:6 Pent:Et_2O) to afford **3n** as a white solid (43 mg, 96%). The spectroscopic data match those previously reported in the literature:[41] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83−7.78 (m, 2H), 7.58−7.49 (m, 2H), 7.29−7.20 (m, 2H), 7.01−6.96 (m, 2H), 6.89 (s, 1H), 3.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.0, 156.1, 154.7, 129.5, 126.4, 123.7, 123.4, 122.8, 120.6, 114.3, 111.0, 99.7, 76.6, 55.4.

*4-[2-(4-Methoxyphenyl)benzofuran-3-yl]benzonitrile (**3nd**).* Following general procedure GP2 with *o*-alkynylphenol **1n** (45 mg, 0.2 mmol) and aryldiazonium **2d** (173 mg, 0.8 mmol). The crude product was purified by flash column chromatography (100:6 Pent:Et_2O) to afford **3nd** as a colorless oil (7 mg, 11%) and **3n** as a white solid (21 mg, 48%): ^{1}H NMR for **3nd** (400 MHz, $CDCl_3$) δ 7.75−7.73 (m, 2H), 7.64−7.62 (m, 2H), 7.57−7.52 (m, 3H), 7.49−7.47 (m, 1H), 7.37−7.32 (m, 1H), 7.29−7.25 (m, 1H), 6.89 (dd, J = 6.8, 2.0 Hz, 2H), 3.84 (s, 3H); ^{13}C NMR for **3nd** (101 MHz, $CDCl_3$) δ 191.6, 160.3, 154.0, 151.9, 138.5, 132.7, 130.4, 129.2, 128.9, 124.8, 123.3, 122.4, 119.2, 118.9, 114.2, 111.3, 111.0, 55.3; IR (neat) 3053, 2965, 2923, 2848, 2226, 1608, 1507, 1452, 1373, 1302, 1253, 1175, 1111, 1071, 1027, 963, 838, 747, 599 cm^{-1}; HRMS calcd for $[C_{22}H_{15}NNaO_2]^+$ 348.0995, found 348.0982.

*Compound **5of**.* Following general procedure GP2 with *o*-alkynylphenol **1o** (52 mg, 0.2 mmol) and aryldiazonium **2f** (154 mg, 0.8 mmol). The crude product was purified by flash column chromatography (100:1 Pent:Et_2O) to afford ketone **5of** (present in the enol form) as a colorless oil (55 mg, 77%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.15 (s, 1H), 7.81−7.78 (dd, J = 8.1, 1.8 Hz, 1H), 7.62−7.59 (d, J = 8.1 Hz, 1H), 7.49−7.27 (m, 9H), 7.02−6.99 (dd, J = 8.4, 1.2 Hz, 1H), 6.86−6.81 (td, J = 7.2, 1.2 Hz, 1H), 6.13 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.6, 163.4, 142.6, 137.8, 136.8, 130.5, 129.6, 129.2, 128.9, 127.8, 125.6 (q, J_{C-F} = 3.7 Hz), 119.2, 118.9, 118.8, 58.6 (two carbons are missing); ^{19}F NMR (282 MHz, $CDCl_3$) δ −62.57; IR (neat) 2924, 1710, 1640, 1576, 1487, 1447, 1414, 1361, 1321, 1226, 1162, 1119, 1066, 1007, 797, 746, 698, 637 cm^{-1}; HRMS calcd for $[C_{21}H_{15}F_3NaO_2]^+$ 379.0916, found 379.0926.

*Compound **6ob**.* Following general procedure GP2 with *o*-alkynylphenol **1o** (52 mg, 0.2 mmol) and aryldiazonium **2b** (189 mg, 0.8 mmol). The crude product was purified by flash column chromatography (100:3 Pent:Et_2O) to afford enol ether **6ob** as a yellow oil (62.7 mg, 76%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.98 (s, 0.05H), 8.22−8.19 (m, 1.06H), 7.96 (dd, J = 6.9, 1.5 Hz, 0.96H), 7.64−7.61 (m, 1.16H), 7.46−7.36 (m, 3.48H), 7.27−7.22 (m, 1H), 7.11−7.05 (m, 2H), 6.93−6.88 (m, 2H), 6.76−6.70 (m, 1H), 6.03−5.97 (m, 0.96H), 3.58−3.57 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.5, 154.4, 152.7, 146.9, 146.3, 142.9, 131.8, 131.8, 131.6, 130.8 (q, J_{C-F} = 34.1 Hz), 125.3 (q, J_{C-F} = 3.7 Hz), 125.1 (q, J_{C-F} = 4.0 Hz), 124.1, 123.4, 123.3, 120.8, 120.7, 118.9, 118.8, 116.5, 116.4, 57.9, 57.8; ^{19}F NMR (282 MHz, $CDCl_3$) δ −62.59, −62.62; IR (neat) 2935, 2844, 1703, 1586, 1513, 1449, 1406, 1322, 1163, 1114, 1069, 1009,

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843, 753, 701, 639 cm^{-1}; HRMS calcd for $[C_{22}H_{16}F_3NNaO_4]^+$ 438.0924, found 438.0940.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01060.

^1H, ^{13}C, and ^{19}F NMR spectra and GC/MS data for compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: cyril.ollivier@upmc.fr. Fax: (+33) 1-4427-7360.
*E-mail: louis.fensterbank@upmc.fr.

Notes

The authors declare no competing financial interest.

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