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Palladium-Catalyzed Copper-Free Sonogashira Coupling of 2-Bromoarylcarbonyls: Synthesis of Isobenzofurans via One-Pot Reductive Cyclization

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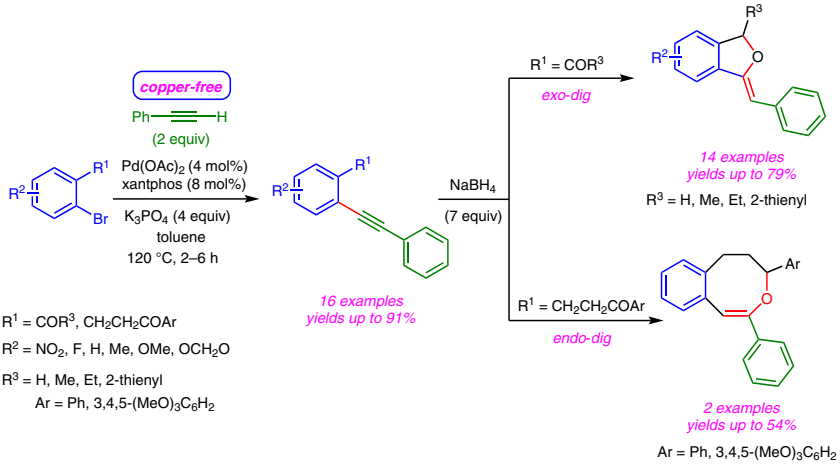

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Abstract Palladium-catalyzed copper-free Sonogashira coupling of 2-bromocarbonyls is presented. This method afforded the 2-alkynylaryl carbonyls, useful synthons for the accomplishment of many carbocyclic and heterocyclic motifs. Significantly, the strategy was extended to the one-pot synthesis of isobenzofurans via reduction followed by intramolecular 5-*exo*-dig cyclization.

Key words carbonyls, alkynes, Sonogashira coupling, isobenzofurans, benzoxocines

2-Alkynylaryl carbonyl compounds are indispensable synthons for the synthesis of various carbocyclic and heterocyclic compounds of natural and unnatural interest. Some of the notable examples include the preparation of indenones,[1] polycyclic indoles,[2] fused pyrrole systems,[3] 3-benzazepines,[4] fused pyrazoles,[5] trifluoromethylated phthalans,[6] isochromenes,[7] isoquinolines,[8] oxazolo-fused pyrroloquinolines,[9] naphthalenes,[10] chrysene derivatives,[11] fluorenes,[12] benzothiophenes,[13] triazolo-heterocyclics,[14] spiro systems,[15] and complex bridged molecules.[16] Consequently, there were reports on the synthesis of 2-alkynylaryl carbonyls via Sonogashira coupling.[17] Most of them were promoted by a dual catalytic systems (palladium catalyst in combination with copper co-catalyst). The use of a copper co-catalyst, rather than being beneficial, sometimes may reduce or completely inhibit the catalytic activity.[18] On the other hand, although copper(I) catalyst alone could promote the Sonogashira coupling, quite often, it affords undesirable diacetylene by-products from acetylenes (Glaser products).[19] Based on such drawbacks, few copper-free Sonogashira couplings have also been developed using solely palladium catalyst or palladium catalyst with some support or with preparation of [Pd]-precatalyst.[20] However, we realized that there is no copper-free general method reported for the preparation of wide range of 2-alkynyl carbonyls. In continuation to our focus on transition metal catalysis and one-pot transformations,[21] very recently, we have described a domino one-pot synthesis of isobenzofurans via copper-catalyzed Sonogashira coupling followed by 5-*exo*-dig cyclization of 2-bromobenzyl tertiary alcohols.[22] However, this copper-catalyzed protocol was unsuccessful with 2-bromobenzyl primary/secondary alcohols. Mostly, it furnished undesired simple oxidized products such as 2-bromoaryl aldehydes/ketones, which is a quite reasonable transformation in the presence of a copper catalyst.[23] Herein, we demonstrate a copper-free Sonogashira coupling of 2-bromoaryl carbonyl compounds for the synthesis of 2-alkynylaryl aldehydes/ketones using a simple palladium catalytic system. Moreover, isobenzofurans were achieved starting from 2-alkynylaryl aldehydes/ketones, using one-pot reduction followed by intramolecular 5-*exo*-dig cyclization.

The synthetic study was initiated with the ketone **1k** and phenylacetylene. Initially, the reaction was performed using well established conditions [i.e., CuI (10 mol%), 1,10-phenanthroline (20 mol%), Cs_2CO_3 (2 equiv) in toluene (0.5 mL) at 110 °C for 24 h].[22] However, no product was formed (Table 1, entry 1) except the formation of undesired diacetylene product. Also, the reaction failed to furnish the prod-

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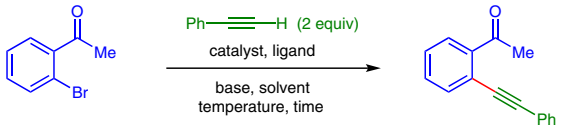
uct in the presence of bases NaHMDS/Cs_2CO_3, different solvents, and at altered temperatures with 10 mol% of CuI (entries 2–8). Interestingly, switching the reaction conditions to $Pd(OAc)_2$ (5 mol%), ligand PPh_3 (10 mol%), base Cs_2CO_3 (4 equiv) in DMF at 80 °C for 4 hours, gave the product **2k**, in fair yield (entry 9). Use of xantphos ligand, under slightly lowered loading of palladium catalyst, improved the yield of **2k** (entry 10). The reaction at relatively high temperature (120 °C) in DMF, suppressed the yield (entry 11), whereas in toluene the yield of product **2k** was increased to 82% (entry 12). Among Cs_2CO_3, K_2CO_3, Na_2CO_3, and K_3PO_4, the base K_3PO_4 was found to be more effective (entries 12–15). Gratifyingly, the reaction in toluene at 120 °C for 2 hours using $Pd(OAc)_2$ (4 mol%), xantphos (8 mol%), and K_3PO_4 (4 equiv) was found to be the best and afforded the 2-alkynyl ketone **2k**, in excellent yield (entry 16).

Among the optimized reaction conditions, the conditions of Table 1, entry 16 were the best, therefore, these conditions were applied for other 2-bromoaryl aldehydes **1a–j** and 2-bromoaryl ketones **1k–n** bearing electron-withdrawing and -donating functionalities on the aromatic ring. Interestingly, the reaction was amenable and furnished the products **2a–n**, in very good to excellent yields (Scheme 1). Notably, the reaction was also successful with electron-withdrawing nitro group (**2j**) and with a heteroaryl moiety (**2n**).

After the successful preparation of alkynes **2**, we aimed to extend our strategy for the synthesis of isobenzofurans via a one-pot reduction followed by 5-*exo*-dig cyclization of **2**. Interestingly, isobenzofuran skeleton comprises prevalent structural motif in small molecules possessing interesting biological and fluorescent properties (Figure 1). For example, *n*-butylphthalide (**3**) is an antiplatelet drug.[24a] The natural product 3-deoxyisochracinic acid (**4**) was isolated from the species of *Cladosporium* that exhibits antibacterial activity by the inhibition of *Bacillus subtilis* growth.[24b] The cyclic ether pestacin (**5**) was isolated from microorganism *Pestalotipsis microspore*, which displays antimycotic, antifungal, and antioxidant activities.[24c] Compound **6** acts as fluorophore with very good light-absorbing efficiency.[24d]

Table 1 Optimization of Reaction Conditions for Sonogashira Coupling of **1k**



1k **2k**

Entry	Ligand (mol%)	Base (equiv)	Solvent	Temp (°C)	Time (h)	Yield (%)[a] of **2k**
1[b]	1,10-phenanthroline (20)	Cs_2CO_3 (2)	toluene	110	24	–[c]
2[b]	1,10-phenanthroline (20)	NaHMDS (4)	toluene	80	12	–[c]
3[b]	–	NaHMDS (4)	toluene	80	12	–[c]
4[b]	1,10-phenanthroline (20)	Cs_2CO_3 (3)	1,4-dioxane	120	12	–[c]
5[b]	1,10-phenanthroline (20)	Cs_2CO_3 (4)	toluene	120	12	–[c]
6[b]	1,10-phenanthroline (20)	Cs_2CO_3 (4)	DMF	150	12	–[c]
7[b]	1,10-phenanthroline (20)	Cs_2CO_3 (4)	DMSO	160	0.5	–[c,d]
8[b]	1,10-phenanthroline (20)	Cs_2CO_3 (4)	MeCN	110	1	–[c,d]
9[e]	PPh_3 (10)	Cs_2CO_3 (4)	DMF	80	2	61
10[f]	xantphos (8)	Cs_2CO_3 (4)	DMF	80	2	78
11[f]	xantphos (8)	Cs_2CO_3 (4)	DMF	120	2	70
12[f]	xantphos (8)	Cs_2CO_3 (4)	toluene	120	2	82
13[f]	xantphos (8)	K_2CO_3 (4)	toluene	120	4	76
14[f]	xantphos (8)	Na_2CO_3 (4)	DMF	120	2	30
15[f]	xantphos (8)	K_3PO_4 (4)	DMF	120	0.75	81
16[f]	**xantphos (8)**	**K_3PO_4(4)**	**toluene**	**120**	**2**	**91**

[a] Isolated yields of chromatographically pure products.
[b] CuI (10 mol%) was used as catalyst.
[c] No significant spot was seen on TLC.
[d] Reaction was performed under microwave conditions.
[e] $Pd(OAc)_2$ (5 mol%) was used as the catalyst.
[f] $Pd(OAc)_2$ (4 mol%) was used as the catalyst.

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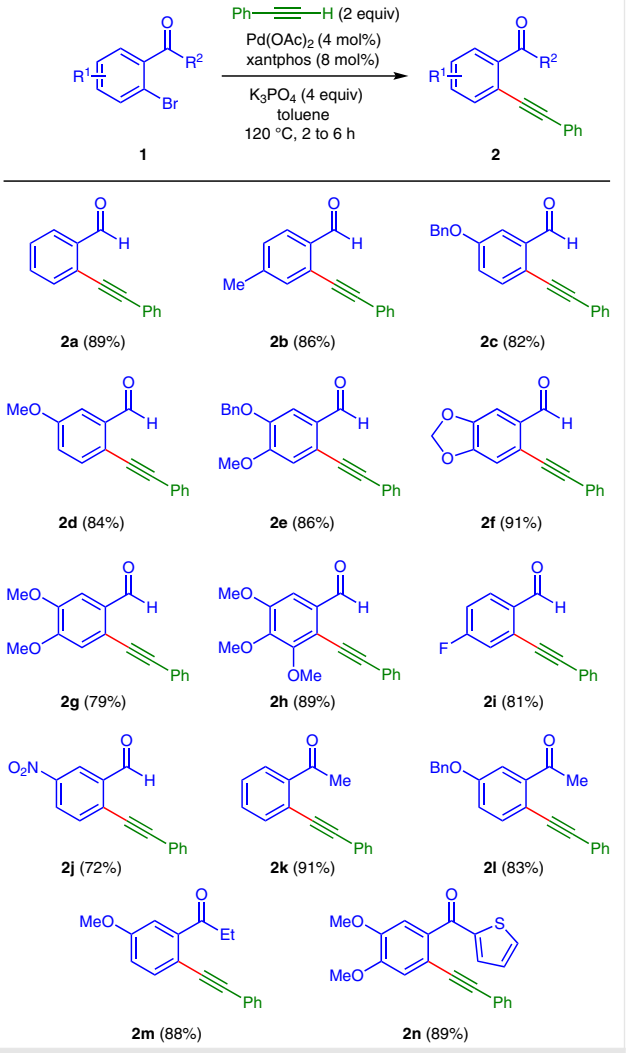


Scheme 1 Scope and generality of the Sonogashira coupling of 2-alkynylaryl aldehydes/ketones **1**. *Reagents and conditions*: Unless otherwise mentioned, all the reactions were carried out by using 2-bromoarylcarbonyl **1** (0.54 mmol), alkyne (1.08 mmol), $Pd(OAc)_2$ (4 mol%), xantphos (8 mol%), and K_3PO_4 (2.16 mmol) followed by toluene (1.0 mL). Yields in parentheses are the isolated yields of chromatographically pure products.

Isobenzofurans are also important building blocks for the synthesis of complex molecules and natural product synthesis.[25]

Due to the above salient features, the synthesis of isobenzofurans has received much attention[26] and we targeted a one-pot preparation of isobenzofurans. Sodium borohydride was chosen as the medium by the assumption that it could promote both reduction as well as intramolecular 5-*exo*-dig cyclization in one pot. Thus, the reaction was performed under different solvents and also at various temperatures (Table 2). To our delight, the reaction with excess sodium borohydride in DMF as a solvent at 110 °C for 24 hours afforded the isobenzofuran **7k** as a single isomer, in very good yield. Further, its structure and stereochemistry were unambiguously confirmed from the reported data.

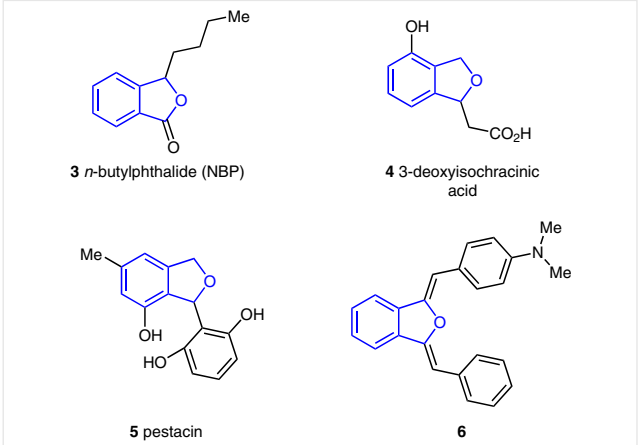
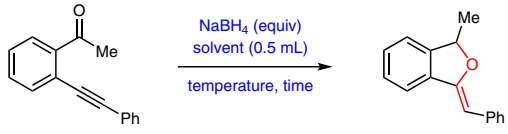


Figure 1 Representative examples of important isobenzofurans

Table 2 Optimization of Reaction Conditions for One-Pot Reductive Cyclization



Entry	$NaBH_4$ (equiv)	Solvent[c]	Temp (°C)	Time (h)	Yield (%)[a] of **7k**
1	2	DMF	80	24	–[b]
2	2	DMF	110	24	–[b]
3	5	DMF	110	24	40
4	7	DMF	110	24	78
5	7	MeOH	70	24	–[b]

[a] Isolated yields of chromatographically pure products.
[b] No product formation, only the reduced alcohol was observed on TLC.
[c] Reduction in toluene was found to be very slow even at 115 °C.

The scope of the one-pot reduction and intramolecular 5-*exo*-dig cyclization was further explored on different 2-alkynylbenzaldehydes/arylketones **2** bearing various functionalities on aromatic ring. Delightfully, the one-pot protocol was quite successful and delivered the isobenzofurans **7**, in fair to good yields (Scheme 2). However, the reaction was unsuccessful with **2j** (neither the starting material nor the product was isolated), maybe due to the more reactive nature of the nitro group.

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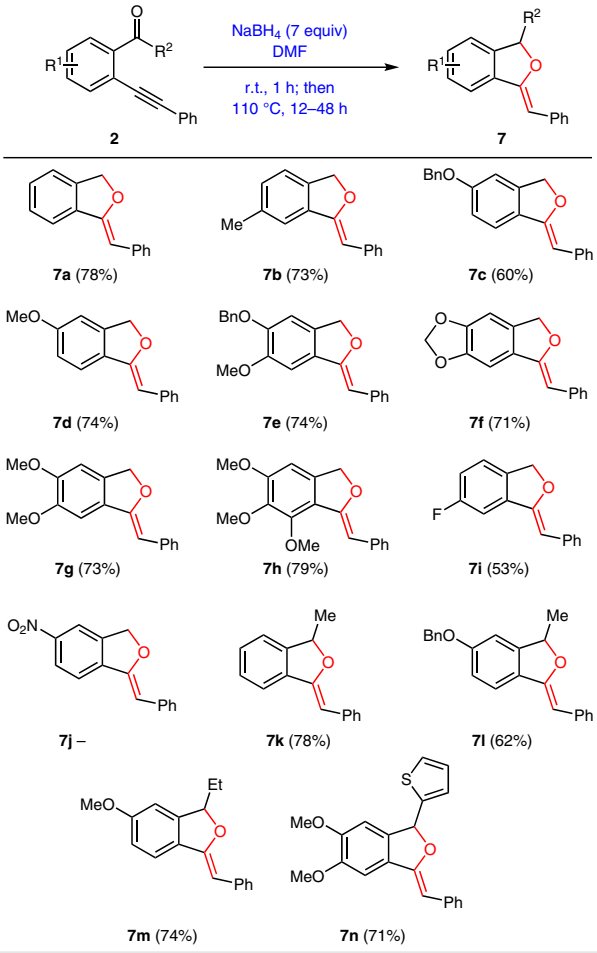
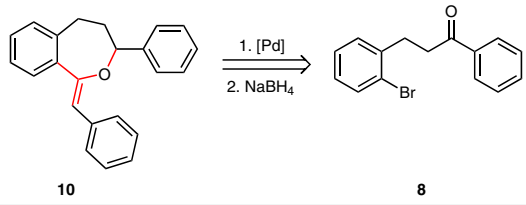


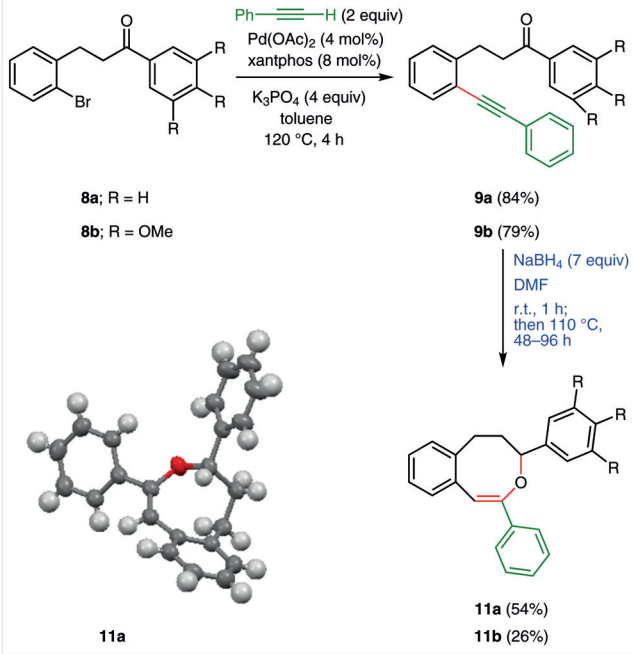
Scheme 2 Scope and generality of the one-pot reductive cyclization to isobenzofurans **7**. *Reagents and conditions*: Unless otherwise mentioned, all the reactions were carried out by using 2-alkynylarylcarbonyls **2** (0.48 mmol), anhyd DMF (0.5 mL) followed by $NaBH_4$ (3.4 mmol). Isolated yields of chromatographically pure products. In the case of **7j**, the reaction was not clean and no significant spot on TLC was noted.

After the synthesis of isobenzofurans, we envisioned that the benzoxepine **10** could be obtained from the bromoketone **8** (Scheme 3). The benzoxepine is an important core unit present in antibacterial natural products.[27] We thought that benzoxepine **10** can be attained using Sonogashira coupling, reduction and *exo*-dig cyclization of ketone **8**. The ketone **8** could be easily synthesized by employing Jeffery–Heck reaction of the corresponding allylic alcohol and 2-bromoiodo derivatives.[21u]

Thus, Sonogashira coupling of ketones **8a** and **8b**, gave the alkynes **9a** and **9b**, in very good yields, respectively. However, the one-pot reduction and cyclization, to our surprise, resulted in the 3-benzoxocines **11a** and **11b** as the major product, respectively, via 8-*endo*-dig cyclization, in poor to moderate yield (Scheme 4). The expected 2-benzoxepine **10** was observed only in minute quantities. The structure of 3-benzoxocine was confirmed by the X-ray crystal data of **11a**.[28] The formation of benzoxocine **11**, as a major product, may be due to the flexibility of side chain of **9**, for the *endo*-dig cyclization. It seems that this protocol for the synthesis of benzoxocine **11** has some limitations, as it was not successful with other systems that were explored under these standard conditions.



Scheme 3 Retrosynthetic approach for the synthesis of 2-benzoxepine **10**



Scheme 4 Synthesis of 3-benzoxocines **11** via Sonogashira coupling followed by one-pot reductive cyclization

Furthermore, we intended to apply the successful conditions of Sonogashira coupling on 2-bromobenzyl 1°/2°/3° alcohols **12** for a possible direct synthesis of isobenzofurans **7**/**13**. However, this approach was quite successful only with 2-bromobenzyl 3° alcohol **12c** and furnished corresponding isobenzofuran **13c** (Scheme 5). This is in analogy to our previous report on copper-catalyzed one-pot synthesis of isobenzofurans starting from 2-bromobenzyl 3° alcohols.[23] In the case of primary and secondary alcohols **12a**

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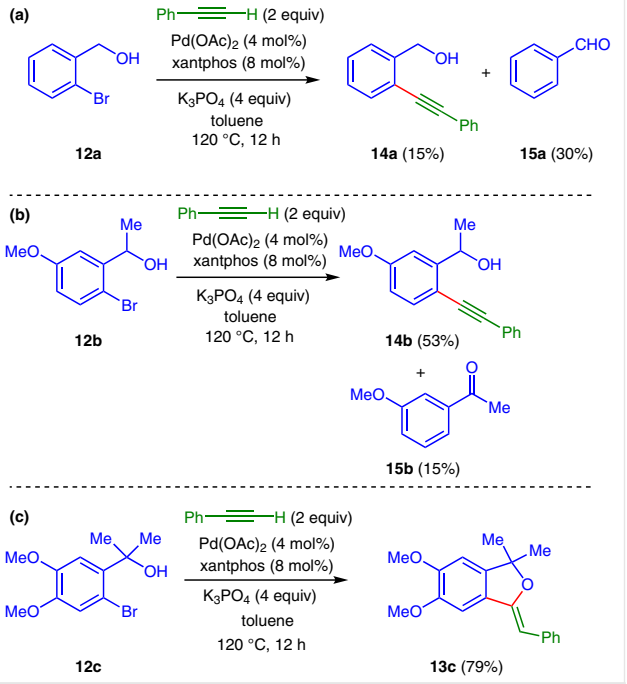
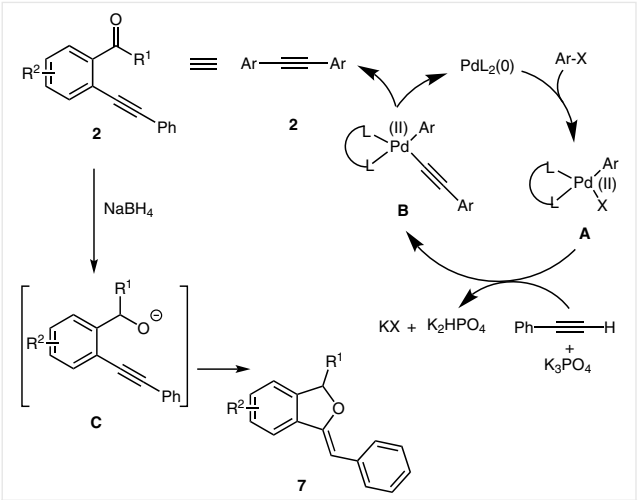
and **12b**, the reaction resulted in the usual oxidation products **15**[21d,i] along with poor to moderate amounts of Sonogashira coupled products **14** (Scheme 5).



Scheme 5 Scope of the direct Sonogashira coupling of 2-bromobenzyl alcohols **12** in the formation of isobenzofurans **7**/**13**

A plausible mechanism for the copper-free Sonogashira coupling and reductive cyclization is outlined in Scheme 6. Initially, the Pd(0) species, is expected to be generated in situ, which would undergo an oxidative addition by insertion of Pd(0) species into the Ar–X (X = Br) bond of 2-bromoaldehyde/ketone and form the aryl Pd(II) intermediate **A**. Subsequent C(sp)–H activation of acetylene via the co-ordination by the displacement of halide in the presence of base would furnish alkynylpalladium(II) species **B**.[29] Further, the intermediate **B** upon reductive elimination would produce the Sonogashira coupled product **2** and regenerate Pd(0) to repeat the catalytic cycle. Additionally, **2** upon reaction with $NaBH_4$ is expected to lead to the one-pot reductive *exo*-dig cyclization via the formation of alkoxide intermediate **C** to generate the isobenzofuran **7**. Similarly, reductive cyclization would lead to benzoxocine **11** from the corresponding precursor **8** in an *endo*-dig manner.

To conclude, we have disclosed a simple palladium-catalyzed copper-free Sonogashira coupling of 2-alkynylaryl carbonyl compounds from readily available 2-bromoaryl derivatives. Significantly, the strategy was extended for the one-pot synthesis of isobenzofurans through reduction followed by intramolecular 5-*exo*-dig cyclization.



Scheme 6 Mechanism for copper-free Sonogashira coupling and one-pot reductive cyclization

IR spectra were recorded on a Bruker Tensor 37 (FTIR) spectrophotometer. ^{1}H NMR spectra were recorded on Bruker Avance 400 (400 MHz) spectrometer at 295 K in $CDCl_3$; chemical shifts (δ ppm) and coupling constants (Hz) are reported in standard fashion with reference to either internal standard TMS (δ_H = 0.00) or residual $CHCl_3$ (δ_H = 7.25). ^{13}C NMR spectra were recorded on Bruker Avance 400 (100 MHz) spectrometer at r.t. in $CDCl_3$; chemical shifts (δ ppm) are reported relative to residual $CHCl_3$ [δ_C = 77.00 (central line of triplet)]. In the ^{13}C NMR, the nature of carbons (C, CH, CH_2, and CH_3) was determined by recording the DEPT-135 spectra, and is given in parentheses and noted as s = singlet (for C), d = doublet (for CH), t = triplet (for CH_2) and q = quartet (for CH_3). In the ^{1}H NMR, standard abbreviations were used throughout. The assignment of signals was confirmed by ^{1}H, ^{13}C CPD, and DEPT spectra. High-resolution mass spectra (HRMS) were recorded on an Agilent 6538 UHD Q-TOF electron spray ionization (ESI) mode and atmospheric pressure chemical ionization (APCI) modes. All small scale dry reactions were carried out using Schlenk tubes under inert atmosphere. Reactions were monitored by TLC on silica gel using a combination of hexane and EtOAc as eluents. Reactions were generally run under argon or N_2 atmosphere. Solvents were distilled prior to use; petroleum ether (PE) with a boiling range of 60 to 80 °C was used. Toluene was dried over sodium metal and DMF was dried over CaH_2. $NaBH_4$ was purchased from local sources (SRL Pvt. Ltd.,) and used as received. Acme silica gel (60–120 mesh) was used for column chromatography (approximately 20 g silica gel/g crude material).

The alkynes **2a**,**b**,**d**,**f**–**k** and compounds **7a**,**b**,**d**,**f**,**g**,**h**,**i**,**k** and **13c** are known in the literature.

Alkynes 2 and 9; General Procedure 1 (GP 1)

In an oven-dried Schlenk tube were added bromoarylcarbonyl **1**/**8** (100.0–204.8 mg, 0.54 mmol), phenylacetylene (110.2 mg, 1.08 mmol), $Pd(OAc)_2$ (4.8 mg, 4 mol%), xantphos (25 mg, 8 mol%), and K_3PO_4 (458 mg, 2.16 mmol) followed by anhyd toluene (1.0 mL) at r.t. under N_2 atmosphere and the reaction mixture was allowed to stir at 120 °C for 2–6 h. Progress of the alkyne **2** and **9** formation was monitored by TLC until the reaction was complete. Then, the mixture was filtered through Celite and washed with CH_2Cl_2. Evaporation of the

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solvent under reduced pressure and purification of the crude material by silica gel column chromatography (PE/EtOAc) furnished the alkyne **2** and **9** (72–91%), respectively, as viscous liquid/semi-solid.

Isobenzofurans 7 and Benzoxocines 11; General Procedure 2 (GP-2)

To an ice cold, magnetically stirred solution of alkyne **2**/**9** (100–192 mg, 0.48 mmol) in anhyd DMF (1 mL), was added $NaBH_4$ (127 mg, 3.36 mmol). Then the reaction mixture was allowed to attain r.t. and stirred for 1 h, then at 110 °C for 12–96 h. Progress of the isobenzofuran **7** and benzoxocine **11** formation was monitored by TLC until the reaction was complete. The reaction mixture was cooled to r.t., treated with ice cold aq NH_4Cl and then extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with brine, dried (Na_2SO_4), and filtered. Evaporation of the filtrate under reduced pressure and purification of the crude material by silica gel column chromatography (PE/EtOAc) furnished the isobenzofuran **7** and benzoxocine **11** (26–79%), respectively. Note: H_2 gas was liberated during the reaction.

5-(Benzyloxy)-2-(phenylethynyl)benzaldehyde (2c)

GP-1 was carried out with benzaldehyde **1c** (157 mg, 0.54 mmol), phenylacetylene (110 mg, 1.08 mmol), $Pd(OAc)_2$ (5 mg, 4 mol%), xantphos (25 mg, 8 mol%), and K_3PO_4 (458 mg, 2.16 mmol) followed by anhyd toluene (1.0 mL) for alkyne **2c** formation at 120 °C for 3 h. Purification of the crude material by silica gel column chromatography (PE/EtOAc, 98:2 to 95:5) furnished the alkyne **2c** (138.5 mg, 82%) as a pale yellow viscous liquid; R_f (**1c**) = 0.60, R_f (**2c**) = 0.50 (PE/EtOAc, 90:10) [UV detection].

IR (MIR-ATR): 3062, 2841, 1688, 1594, 1497, 1454, 1386, 1273, 1163, 1083, 1024, 832 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 10.62 (s, 1 H, CHO), 7.62–7.50 (m, 4 H, ArH), 7.47–7.30 (m, 8 H, ArH), 7.20 (dd, 1 H, *J* = 8.8, 2.9 Hz, ArH), 5.12 (s, 2 H, O*CH*$_2$Ph).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 191.4 (d, CHO), 158.8 (s, Ar-C), 137.1 (s, Ar-C), 135.9 (s, Ar-C), 135.6 (d, Ar-CH), 131.5 (d, 2 C, 2 × Ar-CH), 128.7 (d, Ar-CH), 128.6 (d, 2 C, 2 × Ar-CH), 128.4 (d, 2 C, 2 × Ar-CH), 128.2 (d, Ar-CH), 127.5 (d, 2 C, 2 × Ar-CH), 122.3 (s, Ar-C), 122.2 (d, Ar-CH), 119.7 (s, Ar-C), 110.9 (d, Ar-CH), 94.9 (s, Ar-*C*≡C), 84.8 (s, Ar-C≡*C*), 70.2 (t, O*CH*$_2$Ph).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $[C_{22}H_{17}O_2]^+$: 313.1229; found: 313.1226.

5-(Benzyloxy)-4-methoxy-2-(phenylethynyl)benzaldehyde (2e)

GP-1 was carried out with benzaldehyde **1e** (173 mg, 0.54 mmol), phenylacetylene (110.2 mg, 1.08 mmol), $Pd(OAc)_2$ (4.8 mg, 4 mol%), xantphos (25 mg, 8 mol%), and K_3PO_4 (458 mg, 2.16 mmol) followed by anhyd toluene (1.0 mL) for alkyne **2e** formation at 120 °C for 3 h. Purification of the crude material by silica gel column chromatography (PE/EtOAc, 98:2 to 95:5) furnished the alkyne **2e** (159.2 mg, 86%) as a pale yellow viscous liquid; R_f (**1e**) = 0.60, R_f (**2e**) = 0.50 (PE/EtOAc, 90:10) [UV detection].

IR (MIR-ATR): 3061, 2937, 2839, 1679, 1587, 1503, 1442, 1396, 1350, 1297, 1249, 1162, 1089, 1025, 992, 910, 871, 733 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 10.48 (s, 1 H, CHO), 7.60–7.52 (m, 2 H, Ar-H), 7.48 (s, 1 H, Ar-H), 7.46 (d, 2 H, *J* = 8.3 Hz, Ar-H), 7.42–7.27 (m, 6 H, Ar-H), 7.06 (s, 1 H, Ar-H), 5.18 (s, 2 H, OC*H*2Ph), 3.95 (s, 3 H, Ar-O*CH*$_3$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 190.2 (d, CHO), 154.1 (s, Ar-C), 148.8 (s, Ar-C), 135.9 (s, Ar-C), 131.5 (d, 2 C, 2 × Ar-CH), 130.0 (s, Ar-C), 128.8 (d, Ar-CH), 128.6 (d, 2 C, 2 × Ar-CH), 128.4 (d, 2 C, 2 × Ar-CH), 128.1 (d, Ar-CH), 127.5 (d, 2 C, 2 × Ar-CH), 122.4 (s, Ar-C), 121.6 (s, Ar-C), 114.5 (d, Ar-CH), 110.1 (d, Ar-CH), 94.9 (s, Ar-*C*≡C), 84.8 (s, Ar-C≡*C*), 70.7 (t, O*CH*$_2$Ph), 56.2 (q, Ar-O*CH*$_3$).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $[C_{23}H_{19}O_3]^+$: 343.1329; found: 343.1330.

1-[5-(Benzyloxy)-2-(phenylethynyl)phenyl]ethanone (2l)

GP-1 was carried out with ketone **1l** (164.8 mg, 0.54 mmol), phenylacetylene (110.2 mg, 1.08 mmol), $Pd(OAc)_2$ (4.8 mg, 4 mol%), xantphos (25 mg, 8 mol%), and K_3PO_4 (458 mg, 2.16 mmol) followed by anhyd toluene (1.0 mL) for alkyne **2l** formation at 120 °C for 3 h. Purification of the crude material by silica gel column chromatography (PE/EtOAc, 98:2 to 95:5) furnished the alkyne **2l** (146.3 mg, 83%) as a pale yellow viscous liquid; R_f (**1l**) = 0.60, R_f (**2l**) = 0.50 (PE/EtOAc, 90:10) [UV detection].

IR (MIR-ATR): 3062, 2925, 1679, 1593, 1495, 1322, 1283, 1221, 1206, 1023, 754, 691 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.56 (d, 1 H, *J* = 8.3 Hz, Ar-H), 7.55–7.49 (m, 2 H, Ar-H), 7.47–7.30 (m, 9 H, Ar-H), 7.08 (dd, 1 H, *J* = 8.3, 2.4 Hz, Ar-H), 5.11 (s, 2 H, O*CH*$_2$Ph), 2.81 (s, 3 H, CH_3).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 200.1 (s, C=O), 158.6 (s, Ar-C), 142.1 (s, Ar-C), 136.1 (s, Ar-C), 135.3 (d, Ar-CH), 131.3 (d, 2 C, 2 × Ar-CH), 128.6 (d, 2 C, 2 × Ar-CH), 128.4 (d, Ar-CH), 128.4 (d, 2 C, 2 × Ar-CH), 128.2 (d, Ar-CH), 127.5 (d, 2 C, 2 × Ar-CH), 123.1 (s, Ar-C), 118.6 (d, Ar-CH), 114.2 (s, Ar-C), 114.1 (d, Ar-CH), 93.8 (s, Ar-*C*≡C), 88.4 (s, Ar-C≡*C*), 70.2 (t, O*CH*$_2$Ph), 30.1 (q, CH_3).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $[C_{23}H_{19}O_2]^+$: 327.1380; found: 327.1384.

1-[5-Methoxy-2-(phenylethynyl)phenyl]propan-1-one (2m)

GP-1 was carried out with ketone **1m** (131.3 mg, 0.54 mmol), phenylacetylene (110.2 mg, 1.08 mmol), $Pd(OAc)_2$ (4.8 mg, 4 mol%), xantphos (25 mg, 8 mol%), and K_3PO_4 (458 mg, 2.16 mmol) followed by anhyd toluene (1.0 mL) for alkyne **2m** formation at 120 °C for 2 h. Purification of the crude material by silica gel column chromatography (PE/EtOAc, 98:2 to 95:5) furnished the alkyne **2m** (125.6 mg, 88%) as a pale yellow viscous liquid; R_f (**1m**) = 0.60, R_f (**2m**) = 0.50 (PE/EtOAc, 90:10) [UV detection].

IR (MIR-ATR): 2937, 2837, 1688, 1594, 1496, 1416, 1293, 1276, 1196, 1173, 1025, 823, 755, 691 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.53 (d, 1 H, *J* = 8.8 Hz, Ar-H), 7.53–7.46 (m, 2 H, Ar-H), 7.39–7.30 (m, 3 H, Ar-H), 7.18 (d, 1 H, *J* = 2.9 Hz, Ar-H), 6.98 (dd, 1 H, *J* = 8.8, 2.9 Hz, Ar-H), 3.84 (s, 3 H, ArO*CH*$_3$), 3.20 (q, 2 H, *J* = 7.3 Hz, *CH*$_2$CH$_3$), 1.24 (t, 3 H, *J* = 7.3 Hz, CH$_2$*CH*$_3$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 204.0 (s, C=O), 159.4 (s, Ar-C), 142.7 (s, Ar-C), 135.1 (d, Ar-CH), 131.3 (d, 2 C, 2 × Ar-CH), 128.4 (d, 2 C, 2 × Ar-CH), 128.3 (d, Ar-CH), 123.2 (s, Ar-C), 117.2 (d, Ar-CH), 113.3 (s, Ar-C), 112.8 (d, Ar-CH), 93.1 (s, Ar-*C*≡C), 88.2 (s, Ar-C≡*C*), 55.5 (q, ArO*CH*$_3$), 35.4 (t, *CH*$_2$CH$_3$), 8.5 (q, CH$_2$*CH*$_3$).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $[C_{18}H_{17}O_2]^+$: 265.1223; found: 265.1231.

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[4,5-Dimethoxy-2-(phenylethynyl)phenyl](thien-2-yl)methanone (2n)

GP-1 was carried out with ketone **1n** (176.7 mg, 0.54 mmol), phenylacetylene (110.2 mg, 1.08 mmol), $Pd(OAc)_2$ (4.8 mg, 4 mol%), xantphos (25 mg, 8 mol%), and K_3PO_4 (458 mg, 2.16 mmol) followed by anhyd toluene (1.0 mL) for alkyne **2n** formation at 120 °C for 2 h. Purification of the crude material by silica gel column chromatography (PE/EtOAc, 98:2 to 95:5) furnished the alkyne **2n** (167.5 mg, 89%) as a pale brown viscous liquid; R_f (**1n**) = 0.60, R_f (**2n**) = 0.50 (PE/EtOAc, 90:10) [UV detection].

IR (MIR-ATR): 2933, 2848, 1637, 1593, 1508, 1462, 1411, 1352, 1251, 1211, 1178, 1088, 1029, 728 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.70 (dd, 1 H, *J* = 4.9, 1.0 Hz, Ar-H), 7.60 (dd, 1 H, *J* = 3.9, 1.0 Hz, Ar-H), 7.25–7.18 (m, 3 H, Ar-H), 7.17–7.12 (m, 2 H, Ar-H), 7.09 (dd, 1 H, *J* = 4.9, 3.9 Hz, Ar-H), 7.08 (s, 1 H, Ar-H), 7.07 (s, 1 H, Ar-H), 3.95 (s, 3 H, ArOC*H*$_3$), 3.91 (s, 3 H, ArOC*H*$_3$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 188.1 (s, C=O), 150.4 (s, Ar-C), 148.9 (s, Ar-C), 144.1 (s, Ar-C), 135.6 (d, Ar-CH), 134.6 (s, Ar-C), 134.3 (d, Ar-CH), 131.2 (d, 2 C, 2 × Ar-CH), 128.2 (d, Ar-CH), 128.1 (d, 2 C, 2 × Ar-CH), 128.0 (d, Ar-CH), 122.8 (s, Ar-C), 114.7 (s, Ar-C), 114.6 (d, Ar-CH), 111.4 (d, Ar-CH), 93.6 (s, Ar-C≡C), 87.5 (s, Ar-C≡C), 56.1 (q, ArOCH$_3$), 56.0 (q, ArOCH$_3$).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $[C_{21}H_{17}O_3S]^+$: 349.0893; found: 349.0887.

(1*Z*)-1-Benzylidene-5-(benzyloxy)-1,3-dihydro-2-benzofuran (7c)

GP-2 was carried out with alkyne **2c** (149.9 mg, 0.48 mmol) and anhyd DMF (1 mL), followed by $NaBH_4$ (127 mg, 3.36 mmol) for the formation of isobenzofuran **7c** at 110 °C for 24 h. Purification of the crude material by silica gel column chromatography (PE/EtOAc, 99:1 to 97:3) furnished the isobenzofuran **7c** (90.6 mg, 60%) as a pale yellow viscous liquid; R_f (**2c**) = 0.50, R_f (**7c**) = 0.70 (PE/EtOAc, 90:10) [UV detection].

IR (MIR-ATR): 3032, 2871, 1656, 1610, 1593, 1496, 1449, 1371, 1266, 1228, 1040, 805, 741, 695 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.69 (d, 2 H, *J* = 8.3 Hz, Ar-H), 7.47 (d, 1 H, *J* = 8.3 Hz, Ar-H), 7.45–7.32 (m, 5 H, Ar-H), 7.31 (dd, 2 H, *J* = 7.8, 7.3 Hz, Ar-H), 7.11 (t, 1 H, *J* = 7.3 Hz, Ar-H), 6.99 (dd, 1 H, *J* = 8.3, 2.4 Hz, Ar-H), 6.90 (s, 1 H, Ar-H), 5.80 (s, 1 H, C=CH), 5.46 (s, 2 H, OC*H*$_2$Ar), 5.10 (s, 2 H, OC*H*$_2$Ph).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 159.9 (s, Ar-C), 156.2 (s, *C*=CH), 141.1 (s, Ar-C), 136.6 (s, Ar-C), 136.5 (s, Ar-C), 128.7 (d, 2 C, 2 × Ar-CH), 128.3 (d, 2 C, 2 × Ar-CH), 128.1 (d, Ar-CH), 127.7 (s, Ar-C), 127.4 (2 d, 4 C, 4 × Ar-CH), 124.9 (d, Ar-CH), 121.1 (d, Ar-CH), 116.0 (d, Ar-CH), 106.7 (d, Ar-CH), 94.6 (d, C=*C*H), 74.6 (t, OCH$_2$Ar), 70.4 (t, OCH$_2$Ph).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $[C_{22}H_{19}O_2]^+$: 315.1380; found: 315.1387.

(1*Z*)-1-Benzylidene-5-(benzyloxy)-6-methoxy-1,3-dihydro-2-benzofuran (7e)

GP-2 was carried out with alkyne **2e** (164.3 mg, 0.48 mmol) and anhyd DMF (1 mL), followed by $NaBH_4$ (127 mg, 3.36 mmol) for the formation of isobenzofuran **7e** at 110 °C for 24 h. Purification of the crude material by silica gel column chromatography (PE/EtOAc, 99:1 to 97:3) furnished the isobenzofuran **7e** (122.4 mg, 74%) as a pale yellow viscous liquid; R_f (**2e**) = 0.50, R_f (**7e**) = 0.70 (PE/EtOAc, 90:10) [UV detection].

IR (MIR-ATR): 2928, 1655, 1596, 1500, 1453, 1345, 1287, 1225, 1129 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.70 (dd, 2 H, *J* = 8.3, 1.0 Hz, Ar-H), 7.44 (dd, 2 H, *J* = 8.3, 1.5 Hz, Ar-H), 7.38 (ddd, 2 H, *J* = 8.3, 7.3, 1.5 Hz, Ar-H), 7.31 (dd, 2 H, *J* = 8.3, 7.3 Hz, Ar-H), 7.11 (t, 1 H, *J* = 7.3 Hz, Ar-H), 7.03 (s, 1 H, Ar-H), 6.81 (s, 1 H, Ar-H), 5.77 (s, 1 H, C=CH), 5.38 (s, 2 H, OC*H*$_2$Ar), 5.18 (s, 2 H, OC*H*$_2$Ph), 3.96 (s, 3 H, ArOC*H*$_3$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 156.8 (s, *C*=CH), 150.4 (s, Ar-C), 149.8 (s, Ar-C), 136.6 (s, Ar-C), 136.5 (s, Ar-C), 131.9 (d, Ar-CH), 128.6 (d, 2 C, 2 × Ar-CH), 128.3 (d, 2 C, 2 × Ar-CH), 128.0 (d, Ar-CH), 127.5 (s, Ar-C), 127.4 (d, 2 C, 2 × Ar-CH), 127.2 (d, 2 C, 2 × Ar-CH), 124.9 (d, Ar-CH), 106.1 (d, Ar-CH), 102.6 (d, Ar-CH), 94.5 (d, C=*C*H), 74.7 (t, OCH$_2$Ar), 71.2 (t, OCH$_2$Ph), 56.2 (q, ArOCH$_3$).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $[C_{23}H_{21}O_3]^+$: 345.1485; found: 345.1470.

(1*Z*)-1-Benzylidene-5-(benzyloxy)-3-methyl-1,3-dihydro-2-benzofuran (7l)

GP-2 was carried out with alkyne **2l** (157 mg, 0.48 mmol) and anhyd DMF (1 mL), followed by $NaBH_4$ (127 mg, 3.36 mmol) for the formation of isobenzofuran **7l** at 110 °C for 24 h. Purification of the crude material by silica gel column chromatography (PE/EtOAc, 99:1 to 97:3) furnished the isobenzofuran **7l** (98.1 mg, 62%) as a pale yellow viscous liquid; R_f (**2l**) = 0.50, R_f (**7l**) = 0.70, (PE/EtOAc, 90:10) [UV detection].

IR (MIR-ATR): 3050, 1651, 1596, 1493, 1422, 1271, 1230, 1042, 832, 743 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.73 (d, 2 H, *J* = 8.3 Hz, Ar-H), 7.50–7.34 (m, 6 H, Ar-H), 7.33 (dd, 2 H, *J* = 8.3, 7.3 Hz, Ar-H), 7.12 (t, 1 H, *J* = 7.3 Hz, Ar-H), 6.99 (dd, 1 H, *J* = 8.3, 1.9 Hz, Ar-H), 6.83 (d, 1 H, *J* = 1.9 Hz, Ar-H), 5.78 (s, 1 H, C=CH), 5.69 (q, 1 H, *J* = 6.4 Hz, C*H*CH$_3$), 5.10 (s, 2 H, OC*H*$_2$Ph), 1.62 (q, 3 H, *J* = 6.4 Hz, CHC*H*$_3$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 159.9 (s, Ar-C), 155.3 (s, *C*=CH), 145.7 (s, Ar-C), 136.8 (s, Ar-C), 136.5 (s, Ar-C), 128.6 (d, 2 C, 2 × Ar-CH), 128.3 (d, 2 C, 2 × Ar-CH), 128.1 (d, Ar-CH), 127.5 (s, Ar-C), 127.5 (d, 2 C, 2 × Ar-CH), 127.4 (d, 2 C, 2 × Ar-CH), 124.8 (d, Ar-CH), 121.1 (d, Ar-CH), 115.7 (d, Ar-CH), 106.8 (d, Ar-CH), 94.3 (d, C=*C*H), 81.9 (d, CHCH$_3$), 70.4 (t, OCH$_2$Ph), 21.6 (q, CHCH$_3$).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $[C_{23}H_{21}O_2]^+$: 329.1542; found: 329.1545.

(1*Z*)-1-Benzylidene-3-ethyl-5-methoxy-1,3-dihydro-2-benzofuran (7m)

GP-2 was carried out with alkyne **2m** (127 mg, 0.48 mmol) and anhyd DMF (1 mL), followed by $NaBH_4$ (127 mg, 3.36 mmol) for the formation of isobenzofuran **7m** at 110 °C for 24 h. Purification of the crude material by silica gel column chromatography (PE/EtOAc, 99:1 to 97:3) furnished the isobenzofuran **7m** (94.5 mg, 74%) as a pale yellow viscous liquid; R_f (**2m**) = 0.50, R_f (**7m**) = 0.70 (PE/EtOAc, 90:10) [UV detection].

IR (MIR-ATR): 2958, 1654, 1585, 1489, 1426, 1265, 1221, 846, 738 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.71 (d, 2 H, *J* = 7.8 Hz, Ar-H), 7.45 (d, 1 H, *J* = 8.8 Hz, Ar-H), 7.31 (dd, 2 H, *J* = 7.8, 7.3 Hz, Ar-H), 7.10 (t, 1 H, *J* = 7.3 Hz, Ar-H), 6.90 (dd, 1 H, *J* = 8.8, 1.9 Hz, Ar-H), 6.75 (d, 1 H, *J* = 1.9 Hz, Ar-H), 5.76 (s, 1 H, C=CH), 5.57 (dd, 1 H, *J* = 7.3, 6.8 Hz, C*H*CH-$_2$CH$_3$), 3.85 (s, 3 H, ArOC*H*$_3$), 2.20–1.95 (m, 1 H, CHC*H*-$_a$H-$_b$CH$_3$), 1.90–1.70 (m, 1 H, CHCH-$_a$*H*-$_b$CH$_3$), 1.04 (q, 3 H, *J* = 7.3 Hz, CHCH-$_2$C*H*$_3$).

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^{13}C NMR ($CDCl_3$, 100 MHz): δ = 160.7 (s, Ar-C), 155.6 (s, *C*=CH), 144.3 (s, Ar-C), 136.9 (s, Ar-C), 128.3 (d, 2 C, 2 × Ar-CH), 127.9 (s, Ar-C), 127.4 (d, 2 C, 2 × Ar-CH), 124.7 (d, Ar-CH), 121.1 (d, Ar-CH), 115.0 (d, Ar-CH), 105.9 (d, Ar-CH), 94.0 (d, C=*C*H), 86.6 (d, *C*HCH-$_2$CH$_3$), 55.6 (q, ArO*C*H$_3$), 28.8 (t, CH*C*H-$_2$CH$_3$), 9.0 (t, CHCH-$_2$*C*H$_3$).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for [$C_{18}H_{19}O_2$]$^+$: 267.1385; found: 267.1384.

(1*Z*)-1-Benzylidene-5,6-dimethoxy-3-thien-3-yl-1,3-dihydro-2-benzofuran (7n)

GP-2 was carried out with alkyne **2n** (167 mg, 0.48 mmol) and anhyd DMF (1 mL), followed by $NaBH_4$ (127 mg, 3.36 mmol) for the formation of isobenzofuran **7n** at 110 °C for 24 h. Purification of the crude material by silica gel column chromatography (PE/EtOAc, 99:1 to 97:3) furnished the isobenzofuran **7n** (119.4 mg, 71%) as a pale yellow viscous liquid; R_f (**2n**) = 0.50, R_f (**7n**) = 0.70, (PE/EtOAc 90:10) [UV detection].

IR (MIR-ATR): 3010, 2868, 1649, 1593, 1487, 1381, 1246, 1038, 835, 741 cm^{-1}.

^{1}H NMR (DMSO-d_6, 400 MHz): δ = 7.62 (d, 2 H, *J* = 7.5 Hz, Ar-H), 7.55 (d, 1 H, *J* = 4.4 Hz, Ar-H), 7.37 (s, 1 H, Ar-H), 7.35–7.22 (m, 3 H, Ar-H), 7.15–7.00 (m, 2 H, Ar-H), 6.95 (s, 1 H, Ar-H), 6.87 (s, 1 H, OC*H*Ar), 6.07 (s, 1 H, C=CH), 3.87 (s, 3 H, ArOC*H*$_3$), 3.75 (s, 3 H, ArOC*H*$_3$).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 154.8 (s, *C*=CH), 150.7 (s, Ar-C), 150.1 (s, Ar-C), 143.1 (s, Ar-C), 136.4 (s, Ar-C), 134.1 (s, Ar-C), 128.3 (d, 2 C, 2 × Ar-CH), 127.2 (d, 3 C, 3 × Ar-CH), 127.1 (d, Ar-CH), 126.9 (d, Ar-CH), 125.9 (s, Ar-C), 124.8 (d, Ar-CH), 104.9 (d, Ar-CH), 102.6 (d, Ar-CH), 94.5 (d, C=*C*H), 82.2 (d, O*C*HAr), 55.8 (2 q, 2 C, 2 × ArO*C*H$_3$).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for [$C_{21}H_{19}O_3S$]$^+$: 351.1049; found: 351.1041.

1-Phenyl-3-[2-(phenylethynyl)phenyl]propan-1-one (9a)

GP-1 was carried out with ketone **8a** (155.5 mg, 0.54 mmol), phenylacetylene (110.2 mg, 1.08 mmol), $Pd(OAc)_2$ (4.8 mg, 4 mol%), xantphos (25 mg, 8 mol%), and K_3PO_4 (458 mg, 2.16 mmol) followed by anhyd toluene (0.5 mL) for alkyne **9a** formation at 120 °C for 2 h. Purification of the crude material by silica gel column chromatography (PE/EtOAc, 98:2 to 95:5) furnished the alkyne **9a** (140.6 mg, 84%) as a pale yellow viscous liquid; R_f (**8a**) = 0.60, R_f (**9a**) = 0.50 (PE/EtOAc, 90:10) [UV detection].

IR (MIR-ATR): 3060, 2839, 1685, 1590, 1514, 1455, 1378, 1276, 1160, 1086, 1020, 830 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.97 (dd, 2 H, *J* = 8.3, 1.0 Hz, Ar-H), 7.54 (dd, 1 H, *J* = 7.3, 1.0 Hz, Ar-H), 7.53–7.45 (m, 3 H, Ar-H), 7.38 (dd, 2 H, *J* = 7.8, 7.3 Hz, Ar-H), 7.35–7.30 (m, 4 H, Ar-H), 7.28 (ddd, 1 H, *J* = 7.8, 7.3, 1.5 Hz, Ar-H), 7.22 (ddd, 1 H, *J* = 7.3, 7.3, 1.9 Hz, Ar-H), 3.44–3.36 (m, 2 H, CH_2), 3.35–3.26 (m, 2 H, CH_2).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 199.4 (s, C=O), 143.3 (s, Ar-C), 136.8 (s, Ar-C), 133.0 (d, Ar-CH), 132.3 (d, Ar-CH), 131.5 (d, 2 C, 2 × Ar-CH), 129.2 (d, Ar-CH), 128.6 (d, Ar-CH), 128.5 (d, 2 C, 2 × Ar-CH), 128.4 (d, 2 C, 2 × Ar-CH), 128.3 (d, Ar-CH), 128.1 (d, 2 C, 2 × Ar-CH), 126.3 (d, Ar-CH), 123.2 (s, Ar-C), 122.6 (s, Ar-C), 93.4 (s, Ar-*C*≡C), 87.8 (s, Ar-C≡*C*), 39.5 (t, CH_2), 29.7 (t, CH_2).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for [$C_{23}H_{19}O$]$^+$: 311.1430; found: 311.1425.

3-[2-(Phenylethynyl)phenyl]-1-(3,4,5-trimethoxyphenyl)propan-1-one (9b)

GP-1 was carried out with ketone **8b** (204 mg, 0.54 mmol), phenylacetylene (110.2 mg, 1.08 mmol), $Pd(OAc)_2$ (4.8 mg, 4 mol%), xantphos (25 mg, 8 mol%), and K_3PO_4 (458 mg, 2.16 mmol) followed by anhyd toluene (0.5 mL) for alkyne **9b** formation at 120 °C for 2 h. Purification of the crude material by silica gel column chromatography (PE/EtOAc, 98:2 to 95:5) furnished the alkyne **9b** (170.6 mg, 79%) as a pale yellow viscous liquid; R_f (**8b**) = 0.60, R_f (**9b**) = 0.50 (PE/EtOAc, 90:10) [UV detection].

IR (MIR-ATR): 2959, 2842, 1686, 1576, 1496, 1465, 1380, 1266, 1161, 1056, 1028, 832 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.53 (dd, 1 H, *J* = 7.3, 1.0 Hz, Ar-H), 7.49–7.42 (m, 2 H, Ar-H), 7.34–7.25 (m, 5 H, Ar-H), 7.22 (dd, 1 H, *J* = 7.3, 1.9 Hz, Ar-H), 7.19 (s, 2 H, Ar-H), 3.88 (s, 3 H, ArOC*H*$_3$), 3.83 (s, 6 H, 2 × ArOC*H*$_3$), 3.40–3.34 (m, 2 H, CH_2), 3.33–3.25 (m, 2 H, CH_2).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 198.3 (s, C=O), 153.0 (s, 2 C, 2 × Ar-C), 143.2 (s, Ar-C), 142.4 (s, Ar-C), 132.3 (d, Ar-CH), 132.2 (s, Ar-C), 131.4 (d, 2 C, 2 × Ar-CH), 129.2 (d, Ar-CH), 128.6 (d, Ar-CH), 128.4 (d, 2 C, 2 × Ar-CH), 128.3 (d, Ar-CH), 126.3 (d, Ar-CH), 123.1 (s, Ar-C), 122.6 (s, Ar-C), 105.5 (d, 2 C, 2 × Ar-CH), 93.5 (s, Ar-*C*≡C), 87.7 (s, Ar-C≡*C*), 60.9 (q, ArO*C*H$_3$), 56.2 (q, 2 C, 2 × ArO*C*H$_3$), 39.0 (t, CH_2), 29.7 (t, CH_2).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for [$C_{26}H_{25}O_4$]$^+$: 401.1747; found: 401.1736.

2,4-Diphenyl-5,6-dihydro-4*H*-3-benzoxocine (11a)

GP-2 was carried out with alkyne **9a** (148.8 mg, 0.48 mmol) and anhyd DMF (1 mL), followed by $NaBH_4$ (127 mg, 3.36 mmol) for the formation of benzoxocine **11a** at 110 °C for 24 h. Purification of the crude material by silica gel column chromatography (PE/EtOAc, 99:1 to 97:3) furnished the benzoxocine **11a** (80.9 mg, 54%) as a pale yellow viscous liquid; R_f (**9a**) = 0.50, R_f (**11a**) = 0.70 (PE/EtOAc, 90:10) [UV detection].

IR (MIR-ATR): 3051, 2926, 1652, 1583, 1494, 1453, 1378, 1260, 1030, 836, 741 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.68–7.60 (m, 2 H, Ar-H), 7.40–7.25 (m, 8 H, Ar-H), 7.25–7.10 (m, 4 H, Ar-H), 6.02 (s, 1 H, C=CH), 5.41 (dd, 1 H, *J* = 11.7, 2.9 Hz, *C*HCH$_2$CH$_2$), 3.33 (ddd, 1 H, *J* = 13.2, 13.2, 3.9 Hz, CHCH$_2$*C*H$_a$H$_b$), 2.83 (ddd, 1 H, *J* = 13.2, 4.4, 2.9 Hz, CHCH$_2$CH$_a$*H*$_b$), 2.35–2.15 (m, 1 H, CHC*H*$_a$H$_b$CH$_2$), 1.82 (m, 1 H, CHC*H*$_a$H$_b$CH$_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 155.3 (s, *C*=CH), 142.3 (s, Ar-C), 138.3 (s, Ar-C), 137.5 (s, Ar-C), 136.8 (s, Ar-C), 129.5 (2 d, 2 C, 2 × Ar-CH), 128.5 (d, Ar-CH), 128.3 (d, 2 C, 2 × Ar-CH), 128.1 (d, 2 C, 2 × Ar-CH), 127.5 (d, Ar-CH), 126.9 (d, Ar-CH), 126.5 (d, 2 C, 2 × Ar-CH), 126.3 (d, Ar-CH), 125.9 (d, 2 C, 2 × Ar-CH), 102.1 (d, C=*C*H), 78.5 (d, O*C*HAr), 35.7 (t, CH_2), 31.6 (t, CH_2).

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for [$C_{23}H_{21}O$]$^+$: 313.1587; found: 313.1594.

2,4-Diphenyl-5,6-dihydro-4*H*-3-benzoxocine (11b)

GP-2 was carried out with alkyne **9b** (192 mg, 0.48 mmol) and anhyd DMF (1 mL), followed by $NaBH_4$ (127 mg, 3.36 mmol) for the formation of benzoxocine **11b** at 110 °C for 24 h. Purification of the crude material by silica gel column chromatography (PE/EtOAc, 99:1 to 97:3) furnished the benzoxocine **11b** (50.3 mg, 26%) as a pale yellow viscous liquid; R_f (**9b**) = 0.50, R_f (**11b**) = 0.70 (PE/EtOAc, 90:10) [UV detection].

IR (MIR-ATR): 3045, 2920, 1654, 1588, 1495, 1456, 1380, 1321, 1265, 1036, 841, 739 cm^{-1}.

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^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.70–7.60 (m, 2 H, Ar-H), 7.40–7.30 (m, 3 H, Ar-H), 7.25–7.15 (m, 4 H, Ar-H), 6.58 (s, 2 H, Ar-H), 6.02 (s, 1 H, C=CH), 5.31 (dd, 1 H, *J* = 11.7, 2.4 Hz, $CHCH_2CH_2$), 3.84 (s, 3 H, $ArOCH_3$), 3.84 (s, 6 H, 2 × $ArOCH_3$), 3.33 (ddd, 1 H, *J* = 13.2, 13.2, 3.9 Hz, $CHCH_2CH_aH_b$), 2.90–2.80 (m, 1 H, $CHCH_2CH_aH_b$), 2.30–2.18 (m, 1 H, $CHCH_aH_bCH_2$), 1.90–1.75 (m, 1 H, $CHCH_aH_bCH_2$).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 155.3 (s, C=CH), 153.1 (s, 2 C, 2 × Ar-C), 138.3 (s, Ar-C), 138.0 (s, Ar-C), 137.6 (s, Ar-C), 137.1 (s, Ar-C), 136.7 (s, Ar-C), 129.7 (2 × d, 2 C, 2 × Ar-CH), 128.6 (d, Ar-CH), 128.2 (d, 2 C, 2 × Ar-CH), 127.0 (d, Ar-CH), 126.6 (d, 2 C, 2 × Ar-CH), 126.3 (d, Ar-CH), 102.9 (d, 2 C, 2 × Ar-CH), 102.5 (d, C=CH), 78.7 (d, OCHAr), 60.8 (q, $ArOCH_3$), 56.1 (q, 2 C, 2 × $ArOCH_3$), 35.7 (t, CH_2), 31.6 (t, CH_2).

HRMS (ESI+): *m*/*z* $[M + H]^+$ calcd for $[C_{26}H_{27}O_4]^+$: 403.1909; found: 403.1901.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0036-1588513.

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