

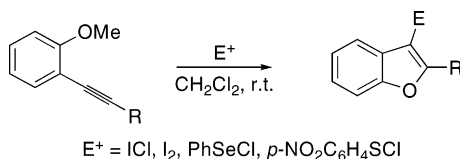
Synthesis of 2,3-Disubstituted Benzo[b]furans by the Palladium-Catalyzed Coupling of *o*-Iodoanisoles and Terminal Alkynes, Followed by Electrophilic Cyclization

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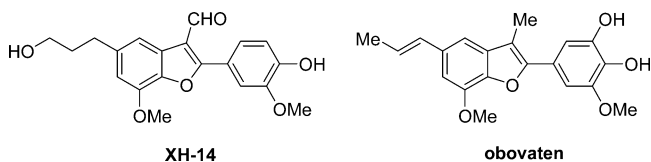


2,3-Disubstituted benzo[b]furans are readily prepared under very mild reaction conditions by the palladium/copper-catalyzed cross-coupling of various *o*-iodoanisoles and terminal alkynes, followed by electrophilic cyclization with I_2 , PhSeCl , or $p\text{-O}_2\text{NC}_6\text{H}_4\text{SCl}$. Aryl- and vinylic-substituted alkynes undergo electrophilic cyclization in excellent yields. Biologically important furopyridines can be prepared by this approach in high yields.

Introduction

The benzo[b]furan nucleus is prevalent in a wide variety of biologically active natural and unnatural compounds.¹ Many 2-arylbenzofuran derivatives are well-known to exhibit a broad range of biological activities, including anticancer,² antiproliferative,³ antiviral,⁴ antifungal,⁵ immunosuppressive,⁶ antiplatelet,⁷ antioxidative,⁸ insecticidal,⁹ antiinflammatory,¹⁰ antifeedant,¹¹ and cancer preventative activity.¹² These compounds are also

important calcium blockers¹³ and phytoestrogens.¹⁴ For instance, XH-14¹⁵ was the first reported potent non-nucleoside adenosine A_1 agonist¹⁶ and obovaten is known as an active antitumor agent.¹⁷

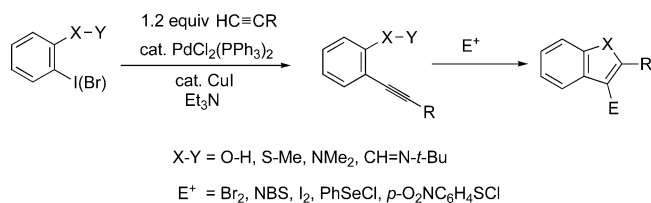


There has been growing interest in developing a general and versatile synthesis of benzo[b]furan derivatives. A number of synthetic approaches to this class of compounds have been introduced in recent years.¹⁸ One common approach to heterocycles that has been utilized for the synthesis of benzo[b]furans,¹⁹ benzo[b]thiophenes,²⁰

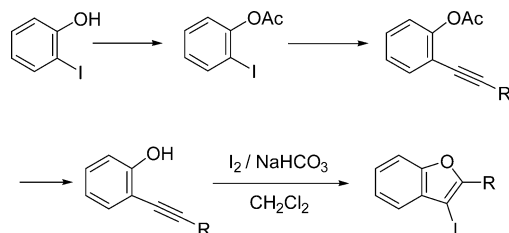
- (1) (a) Dean, F. M. *The Total Synthesis of Natural Products*; ApSimon, J., Ed.; Wiley: New York, 1973; Vol. 1, pp 467–562. (b) Cagniant, P.; Cagniant, D. In *Advances in Heterocyclic Chemistry*; Katritzky, A. R., Boulton, A. J., Eds.; Academic Press: New York, 1975; Vol. 18, pp 337–482. (c) Dean, F. M.; Sargent, M. V. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon Press: Oxford, UK, 1984; Vol. 4, pp 531–596. (d) *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon Press: Oxford, UK, 1996; Vol. 2, pp 259–321.
- (2) (a) Navarro, E.; Alonso, S. J.; Trujillo, J.; Jorge, E.; Perez, C. *J. Nat. Prod.* **2001**, *64*, 134. (b) Lambert, J. D.; Meyers, R. O.; Timmermann, B. N.; Dorr, R. T. *Cancer Lett.* **2001**, *171*, 47. (c) Takasaki, M. T.; Komatsu, K.; Tokuda, H.; Nishino, H. *Cancer Lett.* **2000**, *158*, 53. (d) Banskota, A.; Tezuka, Y.; Midorikawa, K.; Matsushige, K.; Kadota, S. *J. Nat. Prod.* **2000**, *63*, 1277. (e) Lee, S. K.; Cui, B.; Mehta, R. R.; Kinghorn, A. D.; Pezzuto, J. M. *Chem.-Biol. Interact.* **1998**, *115*, 215. (f) Thompson, L. U.; Rickard, S. E.; Orcheson, L. J.; Seidl, M. M. *Carcinogenesis* **1996**, *17*, 1373. (g) Thompson, L. U.; Seidl, M. M.; Rickard, S. E.; Orcheson, L. J.; Fong, H. H. *Nutr. Cancer* **1996**, *26*, 159.
- (3) Ikeda, R.; Nagao, T.; Okabe, H.; Nakano, Y.; Matsunaga, H.; Katano, M.; Mori, M. *Chem. Pharm. Bull.* **1998**, *46*, 871.
- (4) (a) Craig, J.; Callahan, M.; Huang, R. C. C.; DeLucia, A. L. *Antiviral Res.* **2000**, *47*, 19. (b) Leung, C.; Charlton, J. L.; Cow, C. *Can. J. Chem.* **2000**, *78*, 553. (c) Charlton, J. L. *J. Nat. Prod.* **1998**, *61*, 1447.
- (5) (a) Carter, G. A.; Chamberlain, K.; Wain, R. L. *Ann. Appl. Biol.* **1978**, *88*, 57. (b) Zacchino, S.; Rodriguez, G.; Pezzenati, G.; Orellana, G.; Enriz, R.; Gonzalez, S. M. *J. Nat. Prod.* **1997**, *60*, 659.

- (6) (a) Gordaliza, M.; Castro, M.; del Corral, J. M.; Lopez-Vazquez, M.; Feliciano, A. S.; Faircloth, G. T. *Bioorg. Med. Chem. Lett.* **1997**, *7*, 2781. (b) Cho, J. Y.; Kim, A. R.; Yoo, E. S.; Baik, K. U.; Park, M. H. *J. Pharm. Pharmacol.* **1999**, *51*, 1267.
- (7) Chen, C. C.; Hsin, W. C.; Ko, F. N.; Huang, Y. L.; Ou, J. C.; Teng, C. M. *J. Nat. Prod.* **1996**, *59*, 1149.
- (8) (a) Masuda, S.; Hasuda, H.; Tokoroyama, T. *Chem. Pharm. Bull.* **1994**, *42*, 2500. (b) Lu, H.; Liu, G.-T. *Planta Med.* **1992**, *58*, 311. (c) Silva, D. H. S.; Pereira, F. C.; Zanon, M. V. B.; Yoshida, M. *Phytochemistry* **2001**, *57*, 437.
- (9) (a) Findlay, J. A.; Buthelezi, S.; Li, G.; Seveck, M.; Miller, J. D. *J. Nat. Prod.* **1997**, *60*, 1214. (b) Brader, G.; Greger, H.; Bacher, M.; Kalchauer, H.; Hofer, O.; Vajrodarya, S. *J. Nat. Prod.* **1998**, *61*, 1482.
- (10) (a) Day, S. H.; Chiu, N. Y.; Tsao, L. T.; Wang, J. P.; Lin, C. N. *J. Nat. Prod.* **2000**, *63*, 1560. (b) Borsato, M. L. C.; Graef, C. F. F.; Souza, G. E. P.; Lopes, N. P. *Phytochemistry* **2000**, *55*, 809.
- (11) Ward, R. S. *Nat. Prod. Rep.* **1995**, *12*, 183.

SCHEME 1



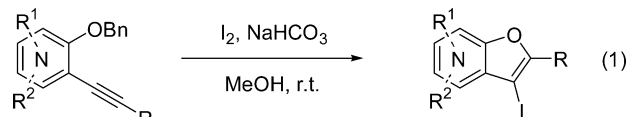
SCHEME 2



indoles,²¹ and isoquinolines²² has been electrophilic cyclization of the corresponding 2-(1-alkynyl)phenols, -thioanisoles, -anilines, and -imines, respectively (Scheme 1).

Our and other's recent success in this area encouraged us to examine the possibility of preparing benzo[b]furans by the same strategy involving a palladium/copper-catalyzed alkyne coupling, followed by electrophilic cyclization. Cacchi and co-workers have previously reported an approach to the synthesis of 3-iodobenzo[b]furans by a related process involving iodocyclization (Scheme 2).¹⁹ Unfortunately, the protecting and deprotecting steps required to synthesize the alkynylphenol are not particularly attractive synthetically. Some of the alkynyl

phenols are also relatively unstable. In another paper, Cacchi has demonstrated an analogous cyclization of benzylic ethers to generate furopyridines and reported that the *o*-hydroxyalkynylpyridines are not stable and cyclize spontaneously to give furopyridines (eq 1).²³ We



have attempted to make this overall approach more attractive synthetically by examining the preparation and cyclization of the corresponding methyl ethers using a variety of commercially available electrophiles. Herein, we wish to report an efficient approach to 2,3-disubstituted benzo[b]furans and furopyridines involving the palladium/copper-catalyzed coupling of various iodoanisoles and an iodomethoxypyridine and terminal alkynes, followed by electrophilic cyclization.

Results and Discussion

The arylalkynes required for our approach to benzo[b]furans are readily prepared by the Sonogashira coupling²⁴ of commercially available *o*-iodoanisoles (5.0 mmol) and terminal alkynes (6.0 mmol) with use of a catalyst consisting of 2 mol % of PdCl₂(PPh₃)₂ and 1 mol % of CuI in the presence of Et₃N (12.5 mL) as the solvent at room temperature. The yields of this process range from 70% to 94% and this procedure should readily accommodate considerable functionality.

We first examined the reaction of our methoxy-substituted aryl alkynes (0.25 mmol in 3 mL of CH₂Cl₂) with I₂ (2.0 equiv in 2 mL of CH₂Cl₂) under our well-established reaction conditions for the synthesis of benzo[b]thiophenes²⁰ and indoles²¹ (Scheme 1). We were pleased to see that 2-(phenylethynyl)anisole reacted in less than 3 h at room temperature to afford 3-iodo-2-phenylbenzo[b]furan in an 87% yield (Table 1, entry 1). To extend this approach to other benzo[b]furans, we have also looked at a range of other readily available electrophiles. So far *p*-O₂NC₆H₄SCl and PhSeCl have been successfully employed in this electrophilic cyclization, providing excellent yields of the desired cyclization products (Table 1, entries 2–4).

The nature of the substituents attached to the triple bond and the arene has a major impact on the success of the reaction. Virtually no difference in the rates of reaction or the overall yields have been observed with use of a vinylic alkyne and arylalkynes bearing certain types of functionality on the aromatic ring (entries 1–16). However, alkynes bearing an alkyl group (entries 19, 20, and 25) fail to undergo electrophilic cyclization. Instead,

(12) (a) den Tonkelaar, I.; Keinan-Boker, L.; Van't Veer, P.; Arts, C. J. M.; Adlercreutz, H.; Thijssen, J. H. H.; Peeters, P. H. M. *Cancer Epidemiol. Biomark. Prev.* **2001**, *10*, 223. (b) Knekt, P.; Adlercreutz, H.; Rissanen, H.; Aromaa, A.; Teppo, L.; Heliovaara, M. *Br. J. Cancer* **2000**, *82*, 1107. (c) Hirose, M.; Lin, C.; Kimoto, N.; Futakuchi, M.; Kono, T.; Nishibe, S.; Shirai, T.; Yamaguchi, T. *Cancer Lett.* **2000**, *155*, 79. (d) Oikannen, S. I.; Pajari, A. M.; Mutanen, M. *Cancer Lett.* **2000**, *159*, 183.

(13) Gubin, J.; de Vogelaer, H.; Inion, H.; Houben, C.; Lucchetti, J.; Mahaux, J.; Rosseels, G.; Peiren, M.; Polstre, P.; Chatelain, P.; Clinet, M. *J. Med. Chem.* **1993**, *36*, 1425.

(14) Pietinen, P.; Stumpf, K.; Mannisto, S.; Kataja, V.; Uusitupa, M.; Adlercreutz, H. *Cancer Epidemiol. Biomark. Prev.* **2001**, *10*, 339.

(15) Chang, H. M.; Cheng, K. P.; Choang, T. F.; Chow, H. F.; Chui, K. Y.; Hon, P. M.; Tan, F. W. L.; Yang, Y.; Zhong, Z. P.; Lee, C. M.; Sham, H. L.; Chan, C. F.; Cui, Y. X.; Wong, H. N. C. *J. Org. Chem.* **1990**, *55*, 3537.

(16) Yang, Z.; Hon, P. M.; Chui, K. Y.; Xu, Z. L.; Chang, H. M.; Lee, C. M.; Cui, Y. X.; Wong, H. N. C.; Poon, C. D.; Fung, B. M. *Tetrahedron Lett.* **1991**, *32*, 2061.

(17) Tsai, I.-L.; Hsieh, C.-F.; Duh, C.-Y. *Phytochemistry* **1998**, *48*, 1371.

(18) (a) Horaguchi, T.; Iwanami, H.; Tanaka, T.; Hasegawa, E.; Shimizu, T.; Suzuki, T.; Tanemura, K. *J. Chem. Soc., Chem. Commun.* **1991**, *44*. (b) Horaguchi, T.; Kobayashi, H.; Miyazawa, K.; Hasegawa, E.; Shimizu, T. *J. Heterocycl. Chem.* **1990**, *27*, 935. (c) Boehm, T. L.; Showalter, H. D. H. *J. Org. Chem.* **1996**, *61*, 6498. (d) Nicolaou, K. C.; Snyder, S. A.; Bigot, A.; Pfefferkorn, J. A. *Angew. Chem., Int. Ed.* **2000**, *39*, 1093. (e) Kondo, Y.; Shiga, F.; Murata, N.; Sakamoto, T.; Yamanaka, H. *Tetrahedron* **1994**, *50*, 11803. (f) Arcadi, A.; Cacchi, S.; Rosario, M. D.; Fabrizi, G.; Marinelli, F. *J. Org. Chem.* **1996**, *61*, 9280. (g) Cacchi, S.; Fabrizi, G.; Moro, L. *Tetrahedron Lett.* **1998**, *39*, 5101. (h) Monteiro, N.; Arnold, A.; Balme, G. *Synlett* **1998**, 1111. (i) Kraus, G. A.; Zhang, N.; Verkade, J. G.; Nagarajan, M.; Kisanga, P. B. *Org. Lett.* **2000**, *2*, 2409. (j) Katritzky, A. R.; Ji, Y.; Fang, Y.; Prakash, I. *J. Org. Chem.* **2001**, *66*, 5613. (k) Kao, C.-L.; Chern, J.-W. *J. Org. Chem.* **2002**, *67*, 6772.

(19) Arcadi, A.; Cacchi, S.; Fabrizi, G.; Marinelli, F.; Moro, L. *Synlett* **1999**, 1432.

(20) (a) Yue, D.; Larock, R. C. *J. Org. Chem.* **2002**, *67*, 1905. (b) Flynn, B. L.; Verdier-Pinard, P.; Hamel, E. *Org. Lett.* **2001**, *3*, 651.

(21) (a) Barluenga, J.; Trincado, M.; Rubio, E.; Gonzalez, J. M. *Angew. Chem., Int. Ed.* **2003**, *42*, 2406. (b) Yue, D.; Larock, R. C. *Org. Lett.* **2004**, *6*, 1037. (c) Amjad, M.; Knight, D. W. *Tetrahedron Lett.* **2004**, *45*, 539.

(22) Huang, Q.; Hunter, J. A.; Larock, R. C. *J. Org. Chem.* **2002**, *67*, 3437.

(23) Arcadi, A.; Cacchi, S.; di Giuseppe, S.; Fabrizi, G.; Marinelli, F. *Org. Lett.* **2002**, *4*, 2409.

(24) (a) Sonogashira, K. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, Germany, 1998; pp 203–229. (b) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467.

TABLE 1. Synthesis of Benzo[*b*]furans by Electrophilic Cyclization^a

entry	alkyne		electrophile	product	% yield	entry	alkyne		electrophile	product	% yield
1		1	I ₂		2 87	15		22	I ₂		23 97
2	1		ICl		2 98						
3	1		PhSeCl		3 100						
4	1		<i>p</i> -O ₂ NC ₆ H ₄ SCl		4 85	16		24	I ₂		25 60
5		5	I ₂		6 80	17		26	I ₂		66 ^c
6	5		PhSeCl		7 88	18	26		PhSeCl		80 ^c
7		8	I ₂		9 100	19		27	I ₂		98 ^c
8	8		PhSeCl		10 96	20	27		PhSeCl		- ^c
9		11	I ₂		12 74	21		28	I ₂		- ^d
10	11		PhSeCl		13 90	22	28		PhSeCl		- ^d
11		14	I ₂		15 80 ^b	23		29	I ₂		- ^d
12		16	I ₂		17 67 ^b	24		30	I ₂		31 68
13		18	I ₂		19 67 ^b	25		32	I ₂		33 66
14		20	I ₂		21 95						

^a All reactions were run with 0.25 mmol of the alkyne and 2 equiv of electrophile in 5 mL of CH₂Cl₂ at 25 °C for 3 h. ^b The reaction took 12 h. ^c None of the desired cyclization product was observed. ^d An inseparable mixture was obtained.

an almost quantitative yield of the product of simple addition of the electrophile to the alkyne triple bond was obtained (entries 19, 20, and 25). To form a furan moiety, the oxygen of the methoxy group has to undergo a five *endo-dig* attack on the carbon–carbon triple bond. The failure to undergo the desired cyclization in entries 19, 20, 21, 22, and 25 is possibly due to more favorable

formation of a “vinylic” cation on the carbon of the triple bond next to the aryl group bearing the methoxy group, instead of on the more remote carbon (see the later mechanistic discussion). Similarly, a methoxy group para to the triple bond increases the electron density on the distal end of the triple bond (Figure 1), which favors electrophilic attack at that position and disfavors a five

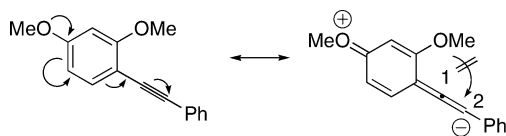


FIGURE 1. Methoxy electron-donating effect on the triple bond.

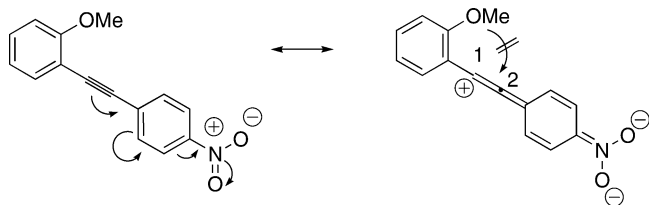


FIGURE 2. Nitro electron-withdrawing effect on the triple bond.

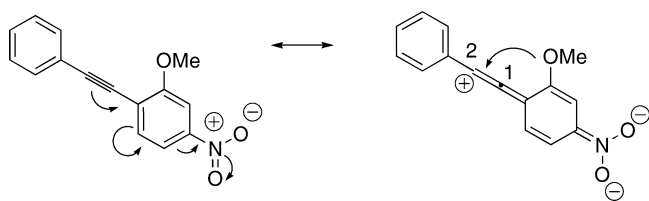


FIGURE 3. Nitro electron-withdrawing effect on the triple bond.

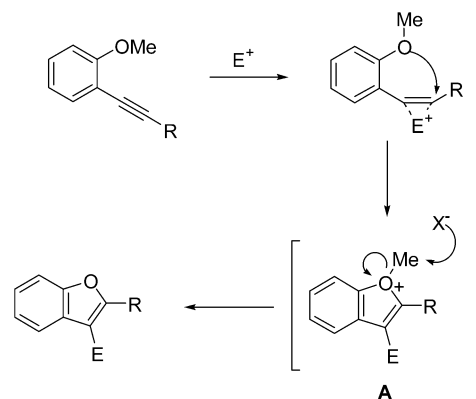
endo-dig cyclization. This, in turn, leads to addition of the electrophile to the triple bond, rather than cyclization (entries 17, 18, and 24).

The presence of a nitro group in compound **28** decreases the electron density on C₁ (Figure 2), and again favors simple addition of the electrophile to the alkyne triple bond (entries 21 and 22). On the other hand, the presence of an electron-withdrawing group, such as a nitro group, on the methoxy-substituted arene favors electrophilic cyclization, although a longer reaction time (12 h) is generally required (entries 11 and 12). The more electron deficient C₂ position is more likely to undergo attack by the nucleophilic oxygen of the methoxy group than the C₁ position, because of either the resonance effect of the nitro group para to the carbon–carbon triple bond (Figure 3) or the inductive effect of the electron-poor arene. The trimethylsilyl-substituted alkyne **29** also failed to undergo electrophilic cyclization, providing instead an inseparable mixture of unidentifiable compounds, which is consistent with Cacchi's earlier results (entry 23).¹⁹

Compound **20** with both a methoxy and an acetoxy group in positions ortho to the triple bond, undergoes exclusive electrophilic cyclization onto the methoxy group to produce compound **21** in a 95% yield (entry 14). This should be quite useful for the regioselective synthesis of benzofurans. Thus, the more nucleophilic methoxy group more readily attacks the triple bond, affording the corresponding cyclization product.

We have also investigated the possibility of carrying out double iodocyclizations, which might be quite useful for the quick assembly of systems with extended conjugation. Compounds **22** and **24** undergo iodocyclization to afford double cyclization products in 97% and 60% yields, respectively (entries 15 and 16).

SCHEME 3



While Cacchi reported the successful synthesis of several furopyridines by electrophilic cyclization of *o*-(benzyloxy)alkynylpyridines, we have examined the cyclization of an *o*-methoxyalkynylpyridine and found that a methyl group can also be a good leaving group in this reaction. Pyridine derivative **18** was treated with I₂ under our standard electrophilic cyclization conditions to afford the desired furopyridine in a 67% yield. This provides a convenient alternative route to the synthesis of furopyridines, since methoxypyridines are more readily available than (benzyloxy)pyridines in many cases.

Mechanistically, we believe that these cyclizations proceed by anti attack of the electrophile and the oxygen of the methoxy group on the alkyne to produce an intermediate **A**, which undergoes methyl group removal via S_N2 displacement by nucleophiles present in the reaction mixture (Scheme 3). In most cases, the nucleophile is presumably the halide remaining in solution.

Conclusions

We believe that this approach to 3-iodobenzo[b]furans and furopyridines should prove quite useful in synthesis, particularly when one considers that there are many ways to transform the resulting iodide functionality into other substituents. For example, the resulting heterocyclic iodides should be particularly useful as intermediates in many palladium-catalyzed processes, like Sonogashira,²⁴ Suzuki,²⁵ and Heck²⁶ cross-coupling processes.

Experimental Section

General. ¹H and ¹³C NMR spectra were recorded at 300 and 75.5 MHz or 400 and 100 MHz, respectively. Thin-layer chromatography was performed with use of commercially prepared 60-mesh silica gel plates (Whatman K6F), and visualization was effected with short-wavelength UV light (254 nm) or a basic KMnO₄ solution [3 g of KMnO₄ + 20 g of K₂CO₃ + 5 mL of NaOH (5%) + 300 mL of H₂O]. All melting points are uncorrected. Low-resolution mass spectra were recorded on a Finnigan TSQ700 triple quadrupole mass

(25) (a) Suzuki, A. *J. Organomet. Chem.* **1999**, 576, 147. (b) Lloyd-Williams, P.; Giralt, E. *Chem. Soc. Rev.* **2001**, 30, 145. (c) Suzuki, A. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, Germany, 1998; pp 49–97. (d) Suzuki, S.; Miyaura, N. *Chem. Rev.* **1995**, 95, 2457.

(26) (a) Crisp, G. T. *Chem. Soc. Rev.* **1998**, 27, 427. (b) Brase, S.; de Meijere, A. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, Germany, 1998; pp 99–166. (c) *Palladium Reagents in Organic Synthesis*; Heck, R. F.; Academic Press: San Diego, CA, 1985; pp 276–287.

spectrometer (Finnigan MAT, San Jose, CA). High-resolution mass spectra were recorded on a Kratos MS50TC double focusing magnetic sector mass spectrometer, using EI at 70 eV.

Reagents. All reagents were used directly as obtained commercially unless otherwise noted. Anhydrous forms of ethyl ether, hexanes, ethyl acetate, and CH_2Cl_2 were purchased from Fisher Scientific Co. 2-Iodoanisole, 2-bromo-1,4-dimethoxybenzene, 1-bromo-2,4-dimethoxybenzene, 2-iodo-4-nitroanisole, 2-iodo-5-nitroanisole, resorcinol, 4-iodoanisole, 1-iodo-4-nitrobenzene, phenylacetylene, 1-cyclohexenyl acetylene, 1-octyne, trimethylsilylacetylene, and Et_3N were purchased from Aldrich Chemical Co., Inc. The palladium salts were donated by Johnson Matthey Inc. and Kawaken Fine Chemicals Co. Ltd.

General Procedure for the Palladium/Copper-Catalyzed Formation of *o*-(1-Alkynyl)anisoles. To a solution of Et_3N (12.5 mL), $\text{PdCl}_2(\text{PPh}_3)_2$ (2 mol %), 5.0 mmol of *o*-iodoanisole, and 6.0 mol of terminal acetylene (stirring for 5 min beforehand) was added CuI (1 mol %) and stirring was continued for another 2 min before flushing with Ar. The flask was then sealed. The mixture was allowed to stir at room temperature for 3–6 h and the resulting solution was filtered, washed with saturated aq NaCl, and extracted with diethyl ether (2×15 mL). The combined ether fractions were dried over anhydrous Na_2SO_4 and concentrated under vacuum to yield the crude product. The crude product was purified by flash chromatography on silica gel with ethyl acetate/hexane as the eluent.

2-(Phenylethynyl)anisole (1). The product was obtained as a yellow oil: ^1H NMR (CDCl_3) δ 3.90 (s, 3H), 6.89 (d, $J = 8.4$ Hz, 1H), 6.93 (t, $J = 7.6$ Hz, 1H), 7.29–7.33 (m, 4H), 7.50 (d, $J = 7.2$ Hz, 1H), 7.55–7.57 (m, 2H); ^{13}C NMR (CDCl_3) δ 56.0, 85.9, 93.6, 110.9, 112.6, 120.7, 123.7, 128.2, 128.3, 129.9, 131.8, 133.7, 160.1; IR (neat, cm^{-1}) 3058, 2926, 2855, 2226; HRMS calcd for $\text{C}_{15}\text{H}_{12}\text{O}$ 208.0888, found 208.0894.

General Procedure for the Iodocyclizations. To a solution of 0.25 mmol of the alkyne and 3 mL of CH_2Cl_2 was added gradually 2 equiv of I_2 dissolved in 2 mL of CH_2Cl_2 . The reaction mixture was flushed with Ar and allowed to stir at room temperature for the desired time. The excess I_2 was removed by washing with saturated aq $\text{Na}_2\text{S}_2\text{O}_3$. The mixture was then extracted by diethyl ether (2×10 mL). The combined

ether layers were dried over anhydrous Na_2SO_4 and concentrated under vacuum to yield the crude product, which was purified by flash chromatography on silica gel with ethyl acetate/hexanes as the eluent.

3-Iodo-2-phenylbenzo[*b*]furan (2). The product was obtained as a yellow oil: ^1H NMR (CDCl_3) δ 7.28–7.51 (m, 7H), 8.16–8.19 (m, 2H); ^{13}C NMR (CDCl_3) δ 61.3, 111.4, 122.1, 123.7, 125.9, 127.7, 128.7, 129.4, 130.2, 132.7, 153.2, 154.1; IR (neat, cm^{-1}) 3058, 1450; HRMS calcd for $\text{C}_{14}\text{H}_9\text{IO}$ 319.9698, found 319.9700.

General Procedure for the *p*- $\text{O}_2\text{NC}_6\text{H}_4\text{SCl}$ and PhSeCl Cyclizations. To a solution of 0.25 mmol of the alkyne and CH_2Cl_2 (5 mL) was added 0.375 mmol of *p*- $\text{O}_2\text{NC}_6\text{H}_4\text{SCl}$ or PhSeCl . The mixture was flushed with Ar and allowed to stir at 25 °C for 2–6 h. The reaction mixture was washed with 20 mL of water and extracted with diethyl ether. The combined ether layers were dried over anhydrous Na_2SO_4 and concentrated under vacuum to yield the crude product, which was further purified by flash chromatography on silica gel with ethyl acetate/hexanes as the eluent.

2-Phenyl-3-(phenylselenyl)benzo[*b*]furan (3). The product was obtained as a yellow oil: ^1H NMR (CDCl_3) δ 7.13–7.17 (m, 3H), 7.22 (t, $J = 4.0$ Hz, 1H), 7.27–7.32 (m, 4H), 7.43 (t, $J = 7.6$ Hz, 2H), 7.51 (d, $J = 8.0$ Hz, 1H), 7.54 (d, $J = 8.0$ Hz, 1H), 8.19–8.21 (m, 2H); ^{13}C NMR (CDCl_3) δ 99.9, 111.4, 121.4, 123.6, 125.4, 126.4, 128.0, 128.7, 129.4, 129.5, 130.3, 131.6, 132.1, 154.3, 157.4; IR (neat, cm^{-1}) 3058, 2926; HRMS calcd for $\text{C}_{20}\text{H}_{14}\text{OSe}$ 350.0211, found 350.0220.

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Supporting Information Available: General experimental details, preparation, iodocyclization, and *p*- $\text{O}_2\text{NC}_6\text{H}_4\text{SCl}$ and PhSeCl cyclizations of *o*-(1-alkynyl)anisoles, and copies of ^1H and ^{13}C NMR spectra. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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