Palladium-Catalyzed Reaction of *o*-Ethynylphenols, *o*-((Trimethylsilyl)ethynyl)phenyl Acetates, and *o*-Alkynylphenols with Unsaturated Triflates or Halides: A Route to 2-Substituted-, 2,3-Disubstituted-, and 2-Substituted-3-acylbenzo[*b*]furans

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The reaction of *o*-ethynylphenols **3** with a wide variety of unsaturated halides or triflates **6** in the presence of $Pd(OAc)_2(PPh_3)_2$, CuI, and Et_3N (procedure A) gives 2-vinyl- and 2-arylbenzo[*b*]furans **7**, in good to high yield, through a palladium-catalyzed coupling followed by an *in situ* cyclization step. Small amounts of 2,3-disubstituted-benzo[*b*]furans **8** are usually isolated as side products. In some cases, however, compounds **8** are generated in significant yield or even as the main products. The formation of **8** can be prevented by employing alternative procedures (B and C) that use *o*-((trimethylsilyl)ethynyl)phenyl acetates **5** as starting building blocks. Procedure B is based on the palladium-catalyzed reaction of **5** with **6** in the presence of $Pd(PPh_3)_4$, Et_3N, and *n*-Bu_4NF, followed by the hydrolysis of the resultant coupling derivative **12** under basic conditions. Procedure C affords **7** through an *in situ* coupling/cyclization of **5** with **6** in the presence of $Pd(PPh_3)_4$ and $KOBu^t$. The utilization of *o*-alkynylphenols **9** as the starting alkynes in the palladium-catalyzed reaction with **6** leads to the formation of 2,3-disubstituted-benzo[*b*]furans **13** through an annulation process promoted by σ-vinyl- and σ-arylpalladium complexes generated *in situ*. The best results in this case are obtained by using KOAc and $Pd(PPh_3)_4$. In the presence of KOAc and $Pd(PPh_3)_4$, and under an atmosphere of carbon monoxide, the reaction of *o*-alkynylphenols with **6** provides 2-vinyl- and 2-aryl-3-acylbenzo[*b*]furans **14**.

Introduction

Alkyne-based palladium-catalyzed reactions provide some of the most versatile and efficient routes to heterocyclic derivatives. Our continuing interest in this area allowed us to develop new synthetic approaches to heterocycles, and a variety of them have been prepared through *in situ* hydroarylation(hydrovinylation)/cyclization reactions,[1] *in situ* coupling/cyclization reactions,[2,3] and annulation reactions promoted by σ-vinyl- and σ-arylpalladium complexes.[4−7] The last two procedures proved very useful for the preparation of functionalized indoles from readily available *o*-ethynylaniline[2b,d] and *o*-alkynyltrifluoroacetanilides.[4b,d,5e] Furthermore, heteroannulations promoted by σ-vinyl- and σ-arylpalladium complexes are extremely valuable since the generation of the indole skeleton combines with the ease of accommodating functionalities amenable to further functional-group manipulation and with a rapid increase in molecular complexity. When such reactions are carried out in the presence of carbon monoxide, one carbon−nitrogen bond and two carbon−carbon bonds are generated in a single synthetic operation.[4d] Considering the structural similarity between indoles and benzo[*b*]furans, it appeared to us that an analogous chemistry might be used

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(1) Arcadi, A.; Bernocchi, E.; Burini, A.; Cacchi, S.; Marinelli, F.; Pietroni, B. *Tetrahedron* **1988**, *44*, 481. Arcadi, A.; Bernocchi, E.; Burini, A.; Cacchi, S.; Marinelli, F.; Pietroni, B. *Tetrahedron Lett.* **1989**, *26*, 3465. Cacchi, S.; Fabrizi, G.; Marinelli, F.; Moro, L.; Pace, P. *Tetrahedron* **1996**, *52*, 10225.

(2) (a) Arcadi, A.; Cacchi, S.; Marinelli, F. *Synthesis* **1986**, 749. (b) Arcadi, A.; Cacchi, S.; Marinelli, F. *Tetrahedron Lett.* **1989**, *30*, 2581. (c) Arcadi, A.; Cacchi, S.; Fabrizi, G.; Marinelli, F. *Synlett* **1993**, 65. (d) Cacchi, S.; Carnicelli, V.; Marinelli, F. *J. Organomet. Chem.* **1994**, *475*, 289.

(3) For other syntheses of heterocycles based on the palladium-catalyzed coupling of 1-alkynes with unsaturated halides or triflates, followed by a cyclization step, see: Tischler, A. N.; Lanza, T. J. *Tetrahedron Lett.* **1986**, *27*, 1653. Sakamoto, T.; Kondo, Y.; Yamanaka, H. *Heterocycles* **1986**, *24*, 31. Sakamoto, T.; Kondo, Y.; Iwashita, S.; Nagano, T.; Yamanaka, H. *Chem. Pharm. Bull.* **1988**, *36*, 1305. Kondo, Y.; Sakamoto, T.; Yamanaka, H. *Heterocycles* **1989**, *29*, 1013. Rudisill, D. E.; Stille, J. K. *J. Org. Chem.* **1989**, *54*, 5856. Neville, C. F.; Barr, S. A.; Grundon, M. F. *Tetrahedron Lett.* **1992**, *33*, 5995. Kumar, V.; Dority, J. A.; Bacon, E. R.; Singh, B.; Lesher, G. Y. *J. Org. Chem.* **1992**, *57*, 6995. Kundu, N. G.; Pal, M. *J. Chem. Soc., Chem. Commun.* **1993**, 86. Candiani, I.; DeBernardinis, S.; Cabri, W.; Marchi, M.; Bedeschi, A.; Penco, S. *Synlett* **1993,** 269. Houpis, I. N.; Choi, W. B., Reider, P. J., Molina, A.; Churchill, H.; Lynch, J.; Volante, R. P. *Tetrahedron Lett.* **1994**, *50*, 9355. Ciufolini, M. A.; Weiss, T. J. *Tetrahedron Lett.* **1994**, *35*, 1127. Kondo, Y.; Shiga, F.; Sakamoto, T.; Yamanaka, H. *Tetrahedron* **1994**, *50*, 11803. Saito, T.; Morimoto, M.; Akiyama, C.; Matsumoto, T.; Suzuki, K. *J. Am. Chem. Soc.* **1995**, *117*, 10757. Shin, K.; Ogasawara, K. *Synlett* **1995**, 859. Liao, H.-Y.; Cheng, C.-H. *J. Org. Chem.* **1995**, *60*, 3711. Bates, R. W.; Rama-Devi, T. *Synlett* **1995**, 1151. Amatore, C.; Blart, E., Genêt, J. P.; Jutand, A.; Lemaire-Audoire, S.; Savignac, M. *J. Org. Chem.* **1995**, *60*, 6829.

(4) (a) Arcadi, A.; Burini, A.; Cacchi, S.; Delmastro, M.; Marinelli, F.; Pietroni, B. R. *J. Org. Chem.* **1992**, *57*, 976. (b) Arcadi, A.; Cacchi, S.; Marinelli, F. *Tetrahedron Lett.* **1992**, *33*, 3915. (c) Arcadi, A.; Cacchi, S.; Larock, R. C.; Marinelli, F. *Tetrahedron Lett.* **1993**, *34*, 2813. (d) Arcadi, A.; Cacchi, S.; Carnicelli, V.; Marinelli, F. *Tetrahedron* **1994**, *50*, 437.

(5) For other syntheses of heterocycles from alkynes promoted by σ-C_{sp^2}-palladium complexes, see: (a) Inoue, Y.; Itoh, Y.; Imaizumi, Y.; Imaizumi, S. *J. Mol. Catal.* **1990**, *60*, L1−L3. (b) Luo, F.-T.; Wang, R.-T. *Tetrahedron Lett.* **1992**, *33*, 6835. (c) Luo, F.-T.; Schreuder, I.; Wang, R.-T. *J. Org. Chem.* **1992**, *57*, 2213. (d) Bouyssi, D.; Gore, J.; Balme, G.; Louis, D.; Wallach, J. *Tetrahedron Lett.* **1993**, *34*, 3129. (e) Saulnier, M. G.; Frennesson, D. B.; Deshpande, M. S.; Vyas, D. M. *Tetrahedron Lett.* **1995**, *36*, 7841. (f) Cavicchioli, M.; Bouyssi, D.; Gore, J.; Balme, G. *Tetrahedron Lett.* **1996**, *37*, 1429.

(6) The cyclization of functionalized alkynes can also be promoted by σ-C_{sp}-palladium complexes, as shown in a straightforward synthesis of 5-(*E*)-alkynylidenetetrahydro-2-furanones: Bouyssi, D.; Gore, J.; Balme, G. *Tetrahedron Lett.* **1992**, *33*, 2811.

(7) Important work in the field of cyclizations promoted by σ-C_{sp^2}-palladium complexes has been done even in the carboannulation of alkynes containing carbon nucleophiles near the carbon−carbon triple bond: Fournet, G.; Balme, G.; Van Hemelryck, B.; Gore, J. *Tetrahedron Lett.* **1990**, *31*, 5147. Fournet, G.; Balme, G.; Gore, J. *Tetrahedron* **1991**, *47*, 6293. Bouyssi, D.; Balme, G.; Gore, J. *Tetrahedron Lett.* **1991**, *32*, 6541. Balme, G.; Bouyssi, D. *Tetrahedron* **1994**, *50*, 403.

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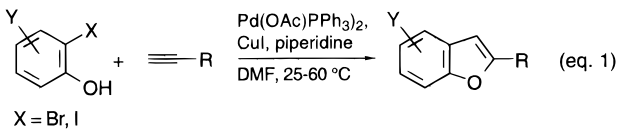
to generate the benzo[*b*]furan skeleton. On the other hand, its occurrence in natural substances and the growing interest in the activity of benzo[*b*]furan derivatives as modulators of androgen biosynthesis (furanosteroids),[8] as inhibitors of 5-lipoxygenase[9] and of the blood coagulation factor Xa,[10] as antagonists of the angiotensin II receptor,[11] as calcium entry blockers,[12] as ligands of adenosine A_1 receptor,[13] as antitumor agents,[14] and as inhibitors of the E-selectin-mediated cell adhesion[15] appear to justify efforts to develop more general and versatile synthetic methodologies to this class of compounds, particularly when these methodologies accommodate considerable functionality and are broad in scope.

Here we report just such a process involving the use of *o*-ethynylphenols **3**, *o*-((trimethylsilyl)ethynyl)phenyl acetates **5**, and *o*-alkynylphenols **9** as building blocks for the synthesis of 2-substituted-, 2,3-disubstituted-, and 2-substituted-3-acylbenzo[*b*]furans.

Results and Discussion

2-Vinyl- and 2-Arylbenzo[*b*]furans 7 from *o*-Ethynylphenols 3 and *o*-((Trimethylsilyl)ethynyl)phenyl Acetates 5. Our palladium-catalyzed reaction of *o*-iodophenols with 1-alkynes represents a very useful procedure for the syntheses of 2-substituted-benzo[*b*]-furans[2a] (eq 1). It allows us in fact to channel the copper-

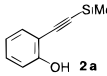
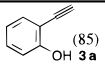
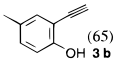
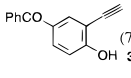
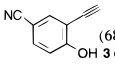
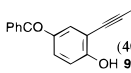
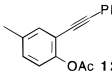
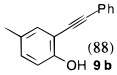
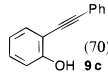
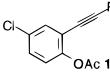
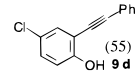
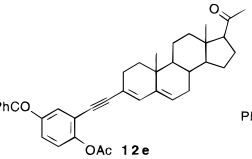
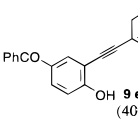
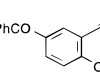
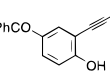


(eq. 1)

mediated synthetic approach to this class of compounds, usually requiring strong conditions (reactions are usually carried out at 110−120 °C),[16] into a mild procedure (reactions are typically carried out at 25−60 °C) that can accommodate a variety of functional groups.

The method, however, is based on the utilization of a specific acetylenic building block for each benzo[*b*]furan, and this may sometimes limit its scope. Therefore, we decided to explore an alternative, more versatile methodology in which several 2-vinyl- and 2-arylbenzo[*b*]-furans can be synthesized from the same acetylenic building block. *o*-Ethynylphenols **3** have been selected as suitable alkynes, and their preparations (Table 1, entries 1−4) have been achieved through the palladium-catalyzed coupling of (trimethylsilyl)acetylene with *o*-iodophenols **1** or *o*-halophenyl acetates **4**, followed by the

Table 1. Preparation of *o*-Ethynylphenols 3 (eq 2) and *o*-Alkynylphenols 9 (eq 7)[a]

entry	**1** and **4**	react. temp./ time (°C/h)	**2**, **5**, and **12** (yield %)	react. temp./ time (°C/h)	**3** and **9** (yield %)
1	 **1a**	45/5[b]	 (96) **2a**	25/3[c]	 (85) **3a**
2	 **1b**	45/6[b]	 (87) **2b**	25/2[c]	 (65) **3b**
3	 **1c**	45/5[b]	 (93) **2c**	25/1[c]	 (75) **3c**
4	 **4a**	80/16[b]	 (75) **5c**	25/2[c]	 (68) **3d**
5	 **4b**	80/5[d]	 (89) **12a**	60/16[e]	 (40) **9a**
6	 **4c**	80/5[d]	 (95) **12b**	60/16[e]	 (88) **9b**
7	 **4d**	80/5[d]	 (73) **12c**	60/5[e]	 (70) **9c**
8	 **2e**	80/2[d]	 (95) **12d**	60/7[e]	 (55) **9d**
9	**4b**	80/4[d]	 (52) **12e**	60/24[e,f]	 **9e** (40)
10	"	60/20[d]	 (67) **12f**	60/20[e]	 **9f** (30)[g]

[a] Yields refer to single runs and are given for pure isolated products. [b] Carried out in dioxane, in the presence of Et_3N, using the following molar ratios: **1** (or **4**):(trimethylsilyl)acetylene: $PdCl_2(PPh_3)_2$:CuI = 1:1.3:0.01:0.02. [c] Carried out in MeOH in the presence of KF (3.58 equiv). [d] Carried out in DMF, in the presence of Et_3N, using the following molar ratios: **4**:1-alkyne: $Pd(OAc)_2(PPh_3)_2$ = 1:2:0.02. [e] Carried out in an acidic Me_2CO/2 N HCl medium. [f] The alkyne needed for the palladium-catalyzed coupling with **4b** was prepared through the palladium-catalyzed reaction of 17β-acetylandrosta-3,5-dien-3-yl triflate with (trimethylsilyl)acetylene according to ref 17 (77% yield), followed by the desilylation of the resultant coupling derivative [MeOH, room temperature, 6 h, KF (3.6 equiv), 94% yield]. [g] The corresponding 2-substituted-benzo[*b*]furan was isolated in 30% yield.

(8) Kumar, V.; Ackerman, J. A. H.; Alexander, M. D.; Bell, M. R.; Christiansen, R. G.; Dung, J. S.; Jaeger, E. P.; Hermann, J. L., Jr.; Krolski, M. E.; McKloskey, P.; Batzold, F. H.; Juniewicz, P. E.; Reel, J.; Snyder, B. W.; Winneker, R. C. *J. Med. Chem.* **1994**, *37*, 4227.

(9) Ohemeng, K. A.; Apollina, M. A.; Nguyen, V. N.; Schwender, C. F.; Singer, M.; Steber, M.; Ansell, J.; Argentieri, D.; Hageman, W. *J. Med. Chem.* **1994**, *37*, 3663.

(10) Nagahara, T.; Yokoyama, Y.; Inamura, K.; Katakura, S.; Komoriya, S.; Yamaguchi, H.; Hara, T.; Iwamoto, M. *J. Med. Chem.* **1994**, *37*, 1200.

(11) Judd, D. B.; Dowle, M. D.; Middlemiss, D.; Scopes, D. I. C.; Ross, B. C.; Jack, T. I.; Pass, M.; Tranquillini, E.; Hobson, J. E.; Panchal, T. A.; Stuart, P. G.; Paton, J. M. S.; Hubbard, T.; Hilditch, A.; Drew, G. M.; Robertson, M. J.; Clark, K. L.; Travers, A.; Hunt, A. A. E.; Polley, J.; Eddershaw, P. J.; Bayliss, M. K.; Manchee, G. R.; Donnelly, M. D.; Walker, D. G.; Richards, S. A. *J. Med. Chem.* **1994**, *37*, 3108. Kiyama, R.; Homna, T.; Hayashi, K.; Ogawa, M.; Hara, M.; Fujimoto, M.; Fujishita, T. *J. Med. Chem.* **1995**, *38*, 2728.

(12) Kozikowsky, A. P.; Ma, D.; Du, L.; Lewin, N. E.; Blumberg, P. M. *Farmaco* **1995**, *50*, 425. Gubin, J.; de Vogelaer, H.; Inion, H.; Houben, C.; Lucchetti, J.; Mahaux, J.; Rosseels, G.; Peiren, M.; Clinet, M.; Polster, P.; Chatelain, P. *J. Med. Chem.* **1993**, *36*, 1425. Kozikowsky, A. P.; Ma, D.; Du, L.; Lewin, N. E.; Blumberg, P. M. *J. Am. Chem. Soc.* **1995**, *117*, 6666.

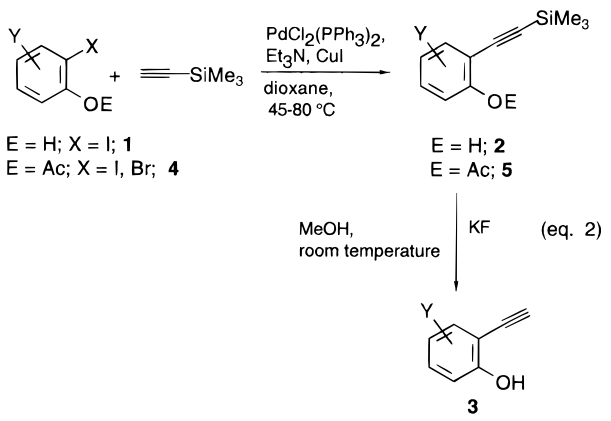
(13) Yang, Z.; Liu, H. B.; Lee, C. M.; Chang, H. M.; Wong, H. N. C. *J. Org. Chem.* **1992**, *57*, 7248.

(14) Gangjee, A.; Devraj, R.; McGuire, J. J.; Kisliuk, R. L. *J. Med. Chem.* **1995**, *38*, 3798, 4495.

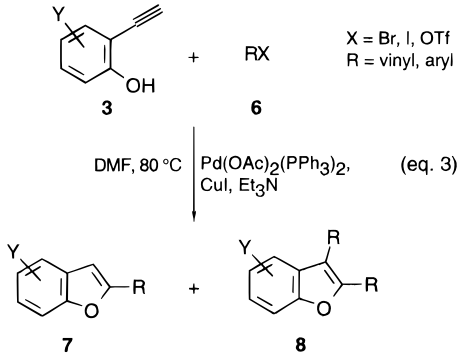
(15) Boschelli, D. H.; Bramer, J. B.; Khtana, S. S.; Sorenson, R. J.; Connor, D. T.; Ferin, M. A.; Wright, C. D.; Lesch, M. E.; Imre, K.; Okonkwo, G. C.; Schrier, D. J.; Conroy, M. C.; Ferguson, E.; Woelle, J.; Saxena, U. *J. Med. Chem.* **1995**, *38*, 4597.

(16) Stephens, R. D.; Castro, C. E. *J. Org. Chem.* **1963**, *28*, 3313. Castro, C. E.; Gaughan, E. J.; Owsley, D. C. *J. Org. Chem.* **1966**, *31*, 4071. Owsley, D. C.; Castro, C. E. *Org. Synth.* **1972**, *52*, 128. Haglund, O.; Nillson, M. *Synlett* **1981**, 671.

desilylation of the resultant (trimethylsilyl)ethynyl derivatives **2** or **5** (under desilylation conditions, the latter undergo even a deacetylation reaction) (eq 2).



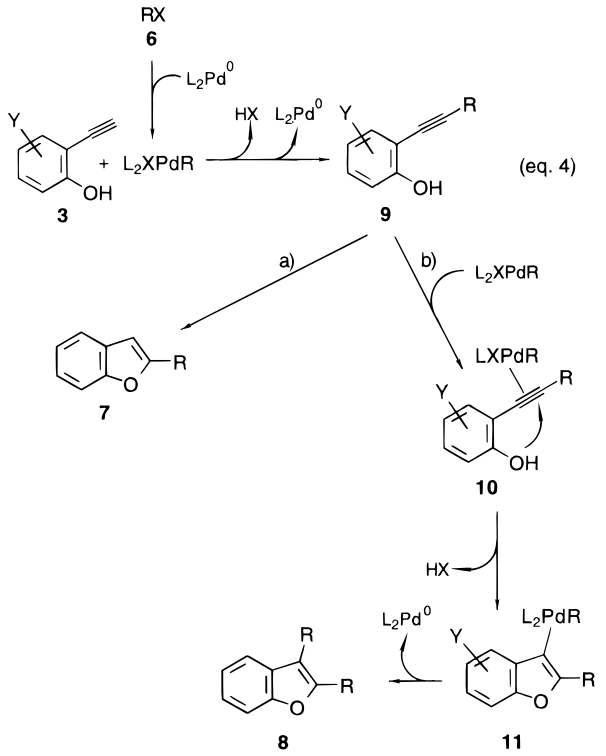
The reaction of **3** with a variety of unsaturated triflates and halides **6** in the presence of $Pd(OAc)_2(PPh_3)_2$ and CuI, according to the conditions reported in eq 3 (procedure A), produced 2-substituted-benzo[*b*]furans **7** in good to high yields (Table 2, entries 1−7). Variable amounts of



2,3-disubstituted-benzo[*b*]furans **8** have been in some cases isolated as side products.

Most probably (eq 4a) compounds **7** arise from the reaction of **3** with "L_2XPdR" complexes (generated *in situ* from zero-valent palladium species and unsaturated triflates or halides), followed by the cyclization of the resultant coupling intermediates **9** through the intramolecular nucleophilic attack of the *ortho* oxygen on the carbon−carbon triple bond. The cyclization step does not seem to require transition metals, as suggested by the observation that *o*-alkynylphenyl acetates **12g** and **12h** can be converted into the corresponding benzo[*b*]furans on treatment with methanol and piperidine (eq 5a). The formation of **8**[4−7] can proceed through (a) coordination of the carbon−carbon triple bond of **9** to σ-C_{sp^2}-palladium complexes to produce the η^2-palladium complexes **10**, (b) intramolecular nucleophilic attack of the *ortho* oxygen onto the activated carbon−carbon triple bond, and (c) reductive deinsertion of Pd^0 species from the resultant σ-vinylpalladium complexes **11** (eq 4b).

The cyclization mechanism not requiring transition metals usually prevails over the competitive palladium-catalyzed annulation leading to **8**. The lone exception to this observation, at least among the substrates we tested, is the reaction of **3a** with 5-bromopyrimidine (Table 2, entry 4). In this case, the main reaction product was the 2,3-bis(5-pyrimidyl)benzo[*b*]furan **8d**, isolated in 33% yield, while 2-(5-pyrimidyl)benzo[*b*]furan was isolated in only 20% yield.

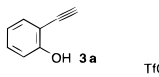
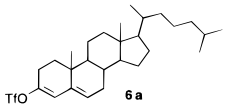
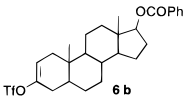
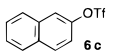
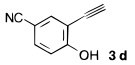
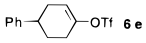
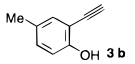
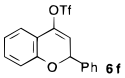
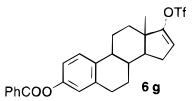
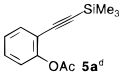
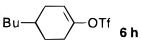
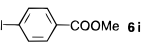
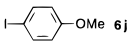
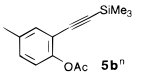
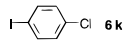
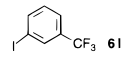


The formation of **8** could be prevented by protecting the hydroxy group as its acetyl derivative during the coupling step. However, the introduction of an additional acylation step after the desilylation of **5** (that, as noted above, deprotects the phenolic group too) or, alternatively, the utilization of a different protecting group, stable under desilylation conditions, would make the procedure more tedious and time consuming. Therefore, we attempted an approach to **7** based on (a) direct palladium-catalyzed coupling of the *o*-((trimethylsilyl)ethynyl)-phenyl acetates **5** with **6** (b) deprotection of the hydroxy group of the resultant *o*-alkynylphenyl acetates **12**, and (c) cyclization (procedure B, eq 5a). This approach has even the advantage of shortening the synthetic process since the compounds **5** are intermediates in the preparation of **3** (eq 2).

The palladium-catalyzed coupling of **5** with **6** has been carried out by employing reaction conditions similar to those reported by us for the carbonylative coupling of 5-((trimethylsilyl)ethynyl)-3′,5′-di-*O*-acetyl-2′-deoxyuridine with aryl halides,[18] and the resulting **12** have been converted into **7** on treatment with piperidine in methanol at 60 °C through a deprotection/cyclization sequence *in situ*. The deprotection/cyclization sequence is very efficient (95−96% yield). However, depending on the parallel hydrolysis of the acetate group (commercially available THF solutions of *n*-Bu_4NF contain significant amounts of water) and on the nature of **6**, the coupling step may produce complex reaction mixtures. For example, treatment of **5a** with **6h** led to the formation of **12h** in 60% yield (**7h** was also isolated in 11% yield) and the overall yield of **7h**, after the deprotection/cyclization step (96% yield) and including the amount generated in the coupling step, was 69% (Table 2, entry 8). A lower yield was instead obtained in the reaction of **5a** with **6d** that afforded the corresponding coupling derivative **12g**

(17) Cacchi, S.; Morera, E.; Ortar, G. *Synthesis* **1986**, 320.

Table 2. Synthesis of 2-Vinyl- and 2-Arylbenzo[*b*]furans 7 (eq 4 and eq 5)

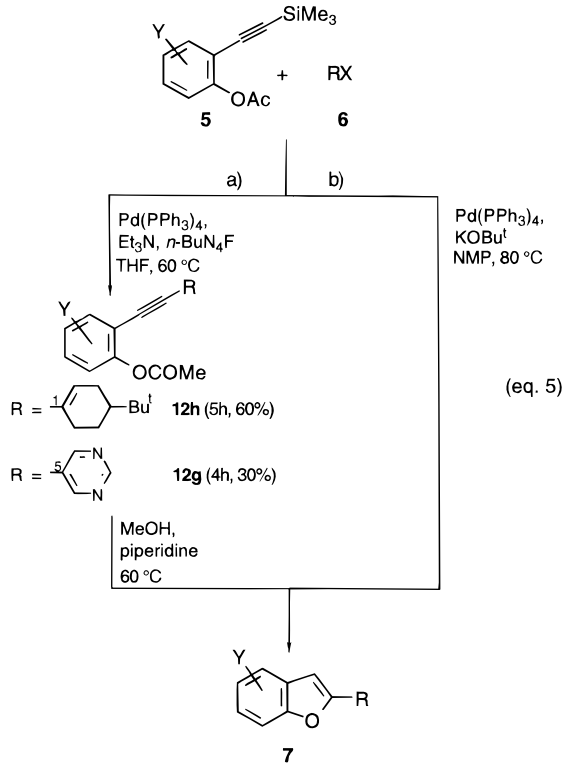
entry	starting alkyne 3 and 5	RX 6	procedure	reaction time (h)	yield % of 7[a]	
1			A[b]	1	78	**7a**
2	"		A[b]	2.5	64	**7b**
3	"		A[b]	5	87	**7c**
4	"		A[b]	4	20[c]	**7d**
5			A[b]	5	42	**7e**
6			A[b]	3,5	50	**7f**
7	"		A[b]	2	72	**7g**
8			B[e]	5[f],1[g]	69[h]	**7h**
9	"	**6d**	B[e]	4[i],2[g]	43[l]	**7d**
10	"	"	C[m]	4	61	**7d**
11	"		C[m]	1	60	**7i**
12	"		C[m]	2	50	**7j**
13			C[m]	1	52	**7k**
14	"		C[m]	1	54	**7l**

[a] Yields refer to single runs and are given for pure isolated products. [b] (DMF, Et_3N, 80 °C) **6**:**3**:$Pd(OAc)_2(PPh_3)_2$:CuI = 1:1.2:0.05:0.05. [c] 2,3-Bis(5-pyrimidyl)benzo[*b*]furan (**8d**) was isolated in 33% yield. [d] Prepared through the acetylation of **2a** in 93% yield. [e] (THF, Et_3N, 60 °C) **6**:**3**:*n*-Bu_4NF:$Pd(PPh_3)_4$ = 1:1.12:1.12:0.02. [f] Reaction time for the coupling step producing **12h** (60% yield) and the corresponding 2-substituted-benzo[*b*]furan **7h** (11% yield). [g] Reaction time for the hydrolysis/cyclization of the coupling derivative **12**. [h] Overall yield, including the amount of **7h** (11%) obtained in the coupling step. [i] Reaction time for the coupling step producing **12g** (30% yield) and the corresponding 2-substituted-benzo[*b*]furan **7d** (15% yield). [l] Overall yield, including the amount of **7d** (15%) obtained in the coupling step. [m] (NMP, 70 °C) **5**:**6**:$KOBu^t$:$Pd(PPh_3)_4$ = 1:1.2:2.2:0.02. [n] Prepared through the acetylation of **2b** in 98% yield.

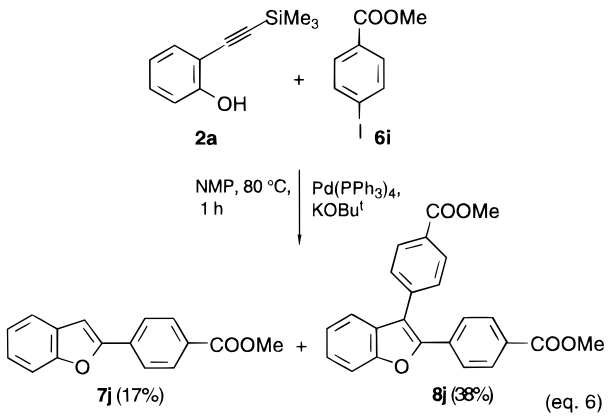
in 30% yield along with a 15% yield of the 2-substituted-benzo[*b*]furan **7d** and other compounds we have not investigated. Compound **12g** was converted into **7d** in 95% yield, and the overall yield, including the amount generated in the coupling step, was in this case 43%.

Better results have been obtained by reacting **5** with **6** in the presence of $KOBu^t$ (less expensive than the THF solution of *n*-Bu_4NF) and $Pd(PPh_3)_4$ in 1-methyl-2-pyrrolidone (NMP) (procedure C, eq 5b).

Under these conditions, *o*-((trimethylsilyl)ethynyl)-phenyl acetates **5** have been converted into **7** in satisfactory yield (Table 2, entries 10−14). For example, the reaction of **5a** with **6d** gave 2-(5-pyrimidyl)benzo[*b*]furan

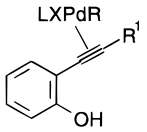


in 61% yield. 2,3-Disubstituted-benzo[*b*]furans **8** have been generated in low yield, most probably because the deprotection of the hydroxy group occurs after the complete, or the near, conversion of the *o*-((trimethylsilyl)ethynyl)phenyl acetate into the corresponding coupling derivative. We have not thoroughly investigated this point. However, the formation of **8j** in 38% yield when **2a**, containing a free hydroxy group, was reacted with **6i** in the presence of $KOBu^t$ appears to support this view (eq 6).



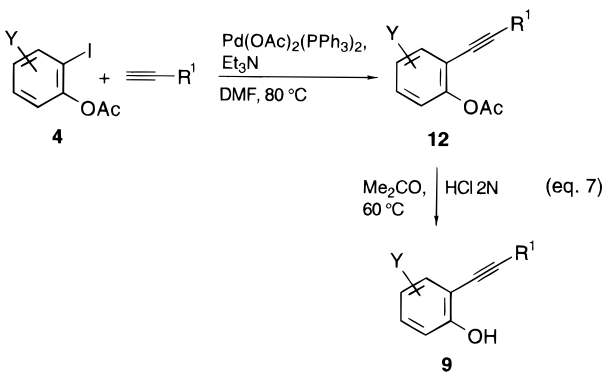
2,3-Disubstituted-benzo[*b*]furans 14 and 2-Vinyl/Aryl-3-acylbenzo[*b*]furans 15 from *o*-Alkynylphenols 9. The development of a procedure for the preparation of 2,3-disubstituted-benzo[*b*]furans **14** starting from *o*-alkynylphenols **9** and unsaturated halides or triflates **6** (eq 8a) has been another target of the present research. The reaction is based on the possible activation of the acetylenic moiety through the formation of the η^2-palladium complex **13** followed by the intramolecular nucleophilic attack of the *ortho* oxygen onto the carbon−carbon triple bond (see the related reaction mechanism for the formation of **8**, eq 4b). Considering that *o*-alkynylphenols **9** have shown a strong tendency to cyclize

to **7** [our present synthesis of 2-substituted-benzo[*b*]-furans (eq 3) is based precisely on it], one of the problems we expected to face when we started this part of the project was to find conditions to allow the cyclization to occur after the formation of **13**.



13

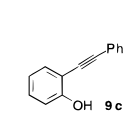
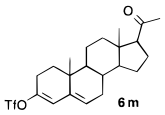
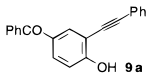
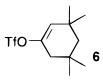
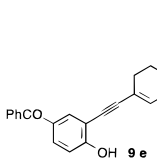
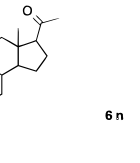
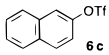
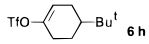
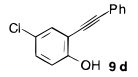
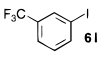
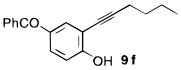
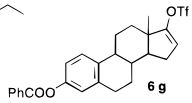
In effect, preventing the intramolecular cyclization of **9** not requiring palladium catalysis was an issue we had to deal with even when we tackled their syntheses. Our approach to their syntheses was in fact based on a two-step procedure involving the palladium-catalyzed reaction of *o*-iodophenyl acetates **4** with 1-alkynes followed by the hydrolysis of the ester group of the resultant coupling products **12**. Alternatively, compounds **12** could be prepared through the palladium-catalyzed coupling of *o*-(trimethylsilyl)ethynyl)phenyl acetates **5** with unsaturated halides or triflates **6** (eq 5a). We knew from the latter that the deprotection of the phenolic oxygen of **12** under basic conditions is followed by a cyclization reaction. Therefore, we attempted the hydrolysis of the ester group under acidic conditions (eq 7) and we were pleased to see that this simple change was enough to allow the conversion of **12** into the desired coupling derivative **9** in satisfactory yield. 2-Substituted-benzo[*b*]furans **7** were usually obtained as side products in small amounts, at least with the examples we investigated. Only with **12f** did the reaction give rise to the formation of an approximate 1/1 mixture of **9f** and of the corresponding 2-substituted-benzo[*b*]furan. Our results are summarized in Table 1 (entries 5−10).



When we next moved to the palladium-catalyzed reaction of **9** with **6**, we examined the effect of a variety of bases, solvents, and catalysts on the reaction outcome, and we arrived at the use of KOAc in the presence of $Pd(PPh_3)_4$ in acetonitrile (procedure D). Under these conditions the desired products **14** have been isolated in satisfactory yields (Table 3, entries 1−5).

Finally, the palladium-catalyzed reaction of **9** with **6** in the presence of KOAc and $Pd(PPh_3)_4$, under a balloon of carbon monoxide (procedure E), produced 2-substituted-3-acylbenzo[*b*]furans **15** (eq 8b), most probably through a mechanism similar to that proposed by us for the formation of 2-substituted-3-acylindoles[4d] (Table 3, entries 6−11). The best results have been achieved with *o*-alkynylphenols bearing electron-withdrawing substituents in the aromatic ring and with vinyl triflates. Depending on the substitution pattern of the reagents,

Table 3. Synthesis of 2,3-Disubstituted-benzo[*b*]furans 14 (eq 8a) and 2-Substituted-3-acylbenzo[*b*]furans 15 (eq 8b) from *o*-Alkynylphenols 9

entry	starting alkyne **9**	RX **6**	procedure	reaction time (h)	yield %[a] of **14**	yield %[a] of **15**
1			D[b]	6	27 **14a**	
2		"	D[b]	3.5	40 **14b**	
3	"		D[b]	2	60 **14c**	
4			D[b]	4	49[c] **14d**	
5	**9a**		D[b]	22	35 **14e**	
6	"	"	E[d]	12	25 **14e**	35 **15a**
7	"	**6m**	E[d]	12		40[e] **15b**
8	"	**6n**	E[d]	12		64 **15c**
9	"		E[d]	12		20[f] **15d**
10		**6n**	E[d]	12		50 **15e**
11	**9d**		E[d]	12		-[g]
12			E[d]	12		-[h]

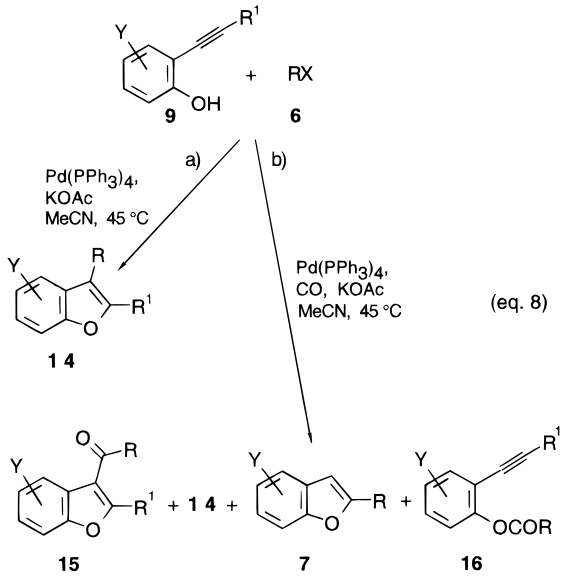
[a] Yields refer to single runs and are given for pure isolated products. [b] (MeCN, 45 °C) **6**:**9**:KOAc:$Pd(PPh_3)_4$ = 1:1:5:0.05. [c] The corresponding 2-substituted-benzo[*b*]furan was isolated in 18% yield. [d] (MeCN, CO, 45 °C) **6**:**9**:KOAc:$Pd(PPh_3)_4$ = 1:1:5:0.05. [e] The corresponding 2-substituted-benzo[*b*]furan was isolated in 20% yield. [f] The corresponding 2-substituted- and 2,3-disubstituted-benzo[*b*]furans were isolated in 19 and 22% yields, respectively. [g] The corresponding *O*-acyl derivative **16a** was isolated in 56% yield. [h] The corresponding 2-substituted-benzo[*b*]furan was isolated in 70% yield.

(18) Arcadi, A.; Cacchi, S.; Marinelli, F.; Pace, P.; Sanzi, G. *Synlett* **1995**, 823.

(19) Anacardio, R.; Arcadi, A.; D'Anniballe, G.; Marinelli, F. *Synthesis* **1995**, 831.

(20) For other palladium-based syntheses of benzo[*b*]furans, see: Hosokawa, T.; Maeda, K.; Koga, K.; Moritani, I. *Tetrahedron Lett.* **1973**, 739. Hosokawa, T.; Ohkata, H.; Moritani, I. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 1533. Cardillo, B.; Cornia, M.; Merlini, L. *Gazz. Chim. Ital.* **1975**, *105*, 1151. Hosokawa, T.; Yamashita, S.; Murahashi, S.-I.; Sonoda, A. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 3662. Pearlman, B. A.; McNamara, J. M.; Hasan, I.; Hatakeyama, S.; Sekizaki, H.; Kishi, Y. *J. Am. Chem. Soc.* **1981**, *103*, 4248. Kondo, Y.; Satoh, M.; Miyaura, N.; Suzuki, A. *Synthesis* **1987**, 373. Larock, R. C.; Stinn, D. E. *Tetrahedron Lett.* **1988**, *29*, 4687. Sakamoto, T.; Yamanaka, H. *Heterocycles* **1989**, *29*, 1013. Villemin, D.; Goussu, D. *Heterocycles* **1989**, *29*, 1255. Iwasaki, M.; Li, J.-P.; Kobayashi, Y.; Matsuzaka, H.; Ishii, Y.; Hidai, M. *Tetrahedron Lett.* **1989**, *30*, 95. Kumar, R. J.; Krupadanam, G. L. D.; Srimannarayana, G. *Synthesis* **1990**, 535. Iwasaki, M.; Kobayashi, Y.; Li, J.-

variable amounts of 2,3-disubstituted-benzo[*b*]furans **14** have also been isolated and in some cases 2-substituted-benzo[*b*]furans **7** have been obtained as the main reaction products (Table 3, entry 12). The presence of electron-donating substituents in the starting *o*-alkynylphenols and/or the utilization of aryl halides resulted in the preferential formation of *O*-acyl derivatives **16**,[19] very likely derived by the capture of acylpalladium intermediates by the phenolic oxygen (Table 3, entry 11).



In conclusion, we have developed new and convenient palladium-based[20] procedures for the construction of the benzo[*b*]furan skeleton that rely on the utilization of readily available acetylenic building blocks and unsaturated triflates or halides. 2-Substituted-benzo[*b*]furan derivatives can be successfully prepared from both *o*-ethynylphenols and *o*-((trimethylsilyl)ethynyl)phenyl acetates. Taking advantage of the features of each methodology, a large number of substituents can be accommodated on the phenolic moiety and on the unsaturated triflate or halide providing access to a large number of 2-substituted-benzo[*b*]furans. We have also shown that a proper choice of the reaction conditions may allow us to control the reactivity of *o*-alkynylphenols so that they can selectively afford 2,3-disubstituted-benzo[*b*]furans through a cyclization reaction promoted by σ-vinyl- and σ-arylpalladium complexes generated *in situ*. In the presence of carbon monoxide the reaction leads to the formation of 2-substituted-3-acylbenzo[*b*]furans. Although yields are in this case only moderate, we believe that this reaction merits attention because it allows us to combine the formation of the carbon−heteroatom bond with the formation of two carbon−carbon bonds; thereby making it possible to prepare a variety of benzo[*b*]furan derivatives not readily available by known procedures.

Experimental Section

Melting points were determined with a Büchi apparatus and are uncorrected. *o*-Hydroxyaryl iodides were prepared according to the procedure given in ref 21. Vinyl triflates were prepared according to ref 22 and were purified by flash chromatography on silica gel eluting with *n*-hexane/EtOAc mixtures. *o*-Iodo- and *o*-bromoaryl acetates **4a**−**e** were prepared in 87−98% yields (on a 4.7−31.0 mmol scale) from the corresponding *o*-halophenols according to standard methods.[23] All of the other starting materials, catalysts, ligands, bases, and solvents (anhydrous solvents included) are commercially available and were used as purchased, without further purification. The palladium-catalyzed conversion of **3**, **9**, and **5** into substituted benzo[*b*]furans **7**, **13**, and **14** was carried out on a 0.3−3 mmol scale. Reaction products were purified by flash chromatography on silica gel eluting with *n*-hexane/EtOAc mixtures.

^{1}H NMR spectra ($CDCl_3$, TMS as internal standard) were recorded at 200 MHz. ^{13}C NMR were recorded at 50.3 MHz. IR spectra were recorded in KBr dispersions unless otherwise indicated.

Typical Procedure for the Preparation of *o*-((Trimethylsilyl)ethynyl)phenols 2 and *o*-((Trimethylsilyl)ethynyl)aryl Acetates 5 and Their Conversion into *o*-Ethynylphenols 3. *o*-((Trimethylsilyl)ethynyl)phenol (2a). To a stirred solution of *o*-iodophenol (8.000 g, 36.36 mmol) and Et_3N (20 mL) in dioxane (20 mL) were added (trimethylsilyl)acetylene (4.640 g, 47.25 mmol), $PdCl_2(PPh_3)_2$ (0.255 g, 0.36 mmol), and CuI (0.140 g, 0.72 mol). The reaction mixture was stirred at 45 °C for 5 h under nitrogen. Diethyl ether and 0.1 N HCl were added, and the organic layer was separated, neutralized with a saturated $NaHCO_3$ solution, washed with water, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by flash chromatography (silica gel, 96/4 *n*-hexane/ethyl acetate) to give **2a** (6.640 g, 96% yield): mp 46−47 °C; IR 3420, 2120, 850, 830, 730 cm^{-1}; ^{1}H NMR δ 7.38−6.80 (m, 4H), 5.99 (s, 1H), 0.31 (s, 9H); ^{13}C NMR δ 157.0, 131.5, 130.5, 120.1, 114.5, 109.4, 102.0, 99.0, −0.16; MS *m*/*e* (relative intensity) 190 (M$^+$, 23), 175 (100). Anal. Calcd for $C_{11}H_{14}OSi$: C, 69.42; H, 7.41. Found: C, 69.54; H, 7.44.

To a stirred solution of **2a** (6.640 g, 0.035 mol) in MeOH (180 mL) was added KF (7.300 g, 0.125 mol). The reaction mixture was stirred for 3 h at room temperature. CH_2Cl_2 and water were added, and, after workup, **3a** was isolated (4.120 g, 85% yield): oil; spectroscopic data are in agreement with those reported in ref 24.

***p*-Methyl-*o*-((trimethylsilyl)ethynyl)phenol (2b):** mp 49−50 °C; IR 3250, 2110, 820 cm^{-1}; ^{1}H NMR δ 7.15−6.80 (m, 4H), 5.69 (s, 1H), 2.22 (s, 3H), 0.25 (s, 9H); ^{13}C NMR δ 154.9, 131.6, 131.4, 129.3, 114.3, 109.0, 101.8, 99.2, 20.2, −0.18; MS *m*/*e* (relative intensity) 204 (M$^+$, 29), 189 (100). Anal. Calcd for $C_{12}H_{16}OSi$: C, 70.53; H, 7.89. Found: C, 70.61; H, 7.86.

***p*-Benzoyl-*o*-((trimethylsilyl)ethynyl)phenol (2c):** oil; IR 3280, 1660, 730, 690 cm^{-1}; ^{1}H NMR δ 7.63−7.35 (m, 8H), 6.93 (s, 1H), −0.3 (s, 9H); ^{13}C NMR δ 196.2, 165.5, 160.1, 138.1, 132.1, 131.8, 129.7, 128.0, 126.7, 124.2, 116.4, 110.9, −2.0; MS *m*/*e* (relative intensity) 294 (M$^+$, 65), 279 (100), 105 (82). Anal. Calcd for $C_{18}H_{18}O_2Si$: C, 73.43; H, 6.16. Found: C, 73.70; H, 6.19.

***o*-((Trimethylsilyl)ethynyl)phenyl acetate (5a):** oil; IR (neat) 2110, 1760, 1350, 840, 820, 730 cm^{-1}; ^{1}H NMR δ 7.58−7.08 (m, 4H), 2.36 (s, 3H), 0.26 (s, 9H); ^{13}C NMR δ 166.4, 151.9, 133.0, 129.5, 125.7, 125.6, 122.0, 117.1, 99.5, 77.0, −0.25; MS *m*/*e* (relative intensity) 232 (M$^+$, 7), 175 (100). Anal. Calcd for $C_{13}H_{16}O_2Si$: C, 67.20; H, 6.94. Found: C, 67.58; H, 6.97.

***p*-Methyl-*o*-((trimethylsilyl)ethynyl)phenyl acetate (5b):** oil; IR (neat) 2120, 1770, 1280, 830, 740 cm^{-1}; ^{1}H NMR δ 7.37−6.98 (m, 3H), 2.37 (s, 3H), 2.35 (s, 3H), 0.30 (s, 9H); ^{13}C NMR δ 166.8, 149.7, 135.4, 133.4, 130.3, 121.7, 116.9, 99.7, 99.0, 20.9, 20.6, −0.11; MS *m*/*e* (relative intensity) 246 (M$^+$, 10), 189 (100), 173 (18). Anal. Calcd for $C_{14}H_{18}O_2Si$: C, 68.25; H, 7.36. Found: C, 68.51; H, 7.39.

P.; Matsuzaka, H.; Ishii, Y.; Hidai, M. *J. Org. Chem.* **1991**, *56*, 1922. Ishii, Y.; Hidai, M. *J. Organomet. Chem.* **1992**, *428*, 279. Dyker, G. *J. Org. Chem.* **1993**, *58*, 6426. Liebeskind, L. S.; Wang, J. *J. Org. Chem.* **1993**, *58*, 3550. Candiani, I.; DeBernardinis, S.; Cabri, W.; Marchi, M.; Bedeschi, A.; Penco, S. *Synlett* **1993**, 269. Larock, R. C.; Yum, E. K.; Doty, M. J.; Sham, K. K. C. *J. Org. Chem.* **1995**, *60*, 3270.

(21) Edgar, K. J.; Falling, S. N. *J. Org. Chem.* **1990**, *55*, 5287.

(22) Stang, P. G.; Treptow, W. *Synthesis* **1980**, 283. Stang, P. G.; Hanack, M.; Subramanian, L. R. *Synthesis* **1982**, 85. Cacchi, S.; Morera, E.; Ortar, G. *Org. Synth.* **1990**, *68*, 138.

(23) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; John Wiley & Sons: 1991; 162−163.

(24) Alberola, A.; Calvo, B.; Ortega, A. G.; Pedrosa, R. *J. Chem. Soc., Perkin Trans. 1* **1992**, 3075.

***p*-Cyano-*o*-((trimethylsilyl)ethynyl)phenyl acetate (5c):** mp 47−48 °C; IR 2200, 2120, 1760, 820 cm^{-1}; ^1H NMR δ 7.76−7.18 (m, 3H), 2.34 (s, 3H), 0.25 (s, 9H); ^{13}C NMR δ 167.5, 154.8, 136.6, 132.8, 124.6, 123.4, 116.9, 109.9, 102.6, 96.9, 20.5, −0.51; MS *m/e* (relative intensity) 257 (M^+, 8), 200 (100), 184 (22). Anal. Calcd for $C_{14}H_{15}NO_2Si$: C, 65.34; H, 5.87; N, 5.44. Found: C, 65.58; H, 5.83; N, 5.49.

***p*-Methyl-*o*-ethynylphenol (3b):** oil; IR (neat) 3500, 3370, 2160, 790 cm^{-1}; ^1H NMR δ 7.04−6.69 (m, 3H), 5.72 (s, 1H), 3.26 (s, 1H), 2.09 (s, 3H); ^{13}C NMR δ 157.0, 134.0, 133.5, 131.4, 116.6, 109.8, 85.7, 80.5, 22.0; MS *m/e* (relative intensity) 132 (M^+, 100), 103 (43). Anal. Calcd for C_9H_8O: C, 81.79; H, 6.10. Found: C, 81.49; H, 6.14.

***p*-Benzoyl-*o*-ethynylphenol (3c):** mp 145−146 °C; IR 3260, 1630, 1370, 820, 690 cm^{-1}; ^1H NMR δ 7.91−7.02 (m, 9H), 3.48 (s, 1H); ^{13}C NMR δ 194.8, 160.9, 137.6, 135.1, 133.3, 132.2, 129.7, 128.3, 128.2, 114.9, 108.5, 85.0, 76.4; MS *m/e* (relative intensity) 222 (M^+, 72), 145 (100), 105 (32). Anal. Calcd for $C_{15}H_{10}O_2$: C, 81.07; H, 4.54. Found: C, 81.38; H, 4.56.

***p*-Cyano-*o*-ethynylphenol (3d):** mp 129−130 °C; IR 3350, 3270, 2200, 875, 805, 760 cm^{-1}; ^1H NMR δ 7.70−7.04 (m, 3H), 6.58 (bs, 1H), 3.57 (s, 1H); ^{13}C NMR δ 160.7, 136.5, 133.3, 118.1, 116.2, 110.0, 104.0, 86.2, 76.2; MS *m/e* (relative intensity) 143 (M^+, 100), 115 (66). Anal. Calcd for C_9H_5NO: C, 75.52; H, 3.52; N, 9.78. Found: C, 75.68; H, 3.48; N, 9.72.

Typical Procedure for the Preparation of *o*-Alkynylphenyl Acetates 12 and *o*-Alkynylphenols 9. *p*-Benzoyl-*o*-(phenylethynyl)phenyl Acetate (12a) and *p*-Benzoyl-*o*-(phenylethynyl)phenol (9a). To a stirred solution of *p*-benzoyl-*o*-acetoxyphenyl iodide (**4b**) (1.670 g, 4.56 mmol) and Et_3N (10 mL) in DMF (2 mL) were added phenylacetylene (0.930 g, 9.12 mmol) and $Pd(OAc)_2(PPh_3)_2$ (0.068 g, 0.09 mmol). The reaction mixture was stirred at 80 °C for 4.5 h under nitrogen. EtOAc and 0.1 N HCl were added, and the organic layer was separated, washed with water, dried (Na_2SO_4), and concentrated under reduced pressure. The residue purified by flash chromatography (silica gel, *n*-hexane) afforded **12a** (1.380 g, 89% yield): mp 106−107 °C; IR 1755, 1660, 1380, 730, 695 cm^{-1}; ^1H NMR δ 8.01−7.26 (m, 13 H), 2.41 (s, 3H); ^{13}C NMR δ 194.8, 166.4, 154.4, 137.1, 135.3, 134.6, 132.7, 131.8, 131.6, 131.0, 126.9, 126.4, 122.4, 121.5, 117.7, 95.1, 93.4, 20.9; MS *m/e* (relative intensity) 340 (M^+, 19), 298 (89), 221 (100). Anal. Calcd for $C_{23}H_{16}O_3$: C, 81.16 ; H, 4.74. Found: C, 80.88; H, 4.71.

12a was dissolved in acetone (25 mL), 2 N HCl (7 mL) was added, and the reaction mixture was stirred for 12 h at 60 °C. Then, EtOAc and water were added, and after workup, the residue was purified by flash chromatography (silica gel, 75/25 v/v *n*-hexane/EtOAc mixture) to give **9a** (0.484 g, 40% yield): mp 139−140 °C; IR 3240, 1630, 1580, 1560, 1500, 1310, 1300, 1260, 810, 745, 690 cm^{-1}; ^1H NMR δ 7.94−7.08 (m, 13H), 7.04 (bs, 1H); ^{13}C NMR δ 195.1, 160.2, 137.6, 134.8, 132.1, 131.6, 129.9, 129.7, 129.0, 128.4, 128.3, 128.2, 121.9, 114.9,-109.9, 96.7, 82.7; MS *m/e* (relative intensity) 298 (M^+, 22), 221 (80), 77(100). Anal. Calcd for $C_{21}H_{14}O_2$: C, 84.54; H, 4.73. Found: C, 81.24; H, 4.70.

***p*-Methyl-*o*-(phenylethynyl)phenyl acetate (12b):** oil; IR (neat) 1760, 1490, 1200, 1180, 810, 740, 670 cm^{-1}; ^1H NMR δ 7.48−6.96 (m, 8H), 2.34 (s, 3H), 2.32 (s, 3H); ^{13}C NMR δ 169.1, 149.3, 135.8, 132.2, 131.5, 130.2, 128.5, 128.4, 126.3, 123.5, 121.9, 116.9, 93.7, 84.4, 20.8, 20.7; MS *m/e* (relative intensity) 250 (M^+, 9), 208 (100), 77 (11). Anal. Calcd for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found: C, 81.29; H, 5.60.

***o*-(Phenylethynyl)phenyl acetate (12c):** mp 36−37 °C; IR 2180, 1760, 1260, 730, 670 cm^{-1}; ^1H NMR δ 7.58−7.08 (m, 9H), 2.34 (s, 3H); ^{13}C NMR δ 166.6, 151.5, 132.8, 131.4, 128.4, 128.3, 125.8, 122.8, 122.2, 122.1, 117.3, 94.1, 84.2; MS *m/e* (relative intensity) 236 (M^+, 11), 194 (100), 165 (45). Anal. Calcd for $C_{16}H_{12}O_2$: C, 81.34; H, 5.12. Found: C, 81.65; H, 5.15.

***p*-Chloro-*o*-(phenylethynyl)phenyl acetate (12d):** mp 53−54 °C; IR 1770, 1275, 730, 675 cm^{-1}; 1H NMR δ 7.53−7.01 (m, 8 H), 2.33 (s, 3H); ^{13}C NMR δ 168.6, 150.0, 132.45, 129.41, 128.9, 128.4, 123.5, 122.3, 119.0, 95.3, 83.0, 20.7; MS *m/e* (relative intensity) 272 (M^+, 3), 270 (M^+, 9), 230 (31), 228 (100). Anal. Calcd for $C_{16}H_{11}ClO_2$: C, 70.99; H, 4.10. Found: C, 70.65; H, 4.07.

***p*-Benzoyl-*o*-((17β-acetylandrosta-3,5-dien-3-yl)ethynyl)-phenyl acetate (12e):** mp 164−165 °C; IR 2160, 1770,1760, 1700, 780, 710, 700 cm^{-1}; ^1H NMR δ 7.91−7.18 (m, 8 H), 6.35 (s, 1H), 5.56 (bs, 1H), 2.36 (s, 3H), 2.12 (s, 3H), 1.05 (s, 3H), 1.84 (s, 3H); ^{13}C NMR δ 209.4, 194.8, 168.2, 154.1, 141.0, 136.5, 134.5, 130.5, 128.9, 127.2, 122.3, 97.5, 83.4; MS *m/e* (relative intensity) 560 (M^+, 6), 518 (6), 105 (100). Anal. Calcd for $C_{38}H_{40}O_4$: C, 81.40; H, 7.19. Found: C, 81.15; H, 7.15.

***p*-Benzoyl-*o*-(hex-1-ynyl)phenyl acetate (12f):** oil; IR 2190, 1765, 1660, 1270, 700 cm^{-1}; ^1H NMR δ 7.89−715 (m, 8H), 2.37 (t, 3H), 2.33 (s, 3 H), 1.52 (m, 4H), 0.92 (t, 3H); ^{13}C NMR δ 194.5, 166.0, 154.3, 136.8, 134.9, 134.6, 132.3, 131.7, 130.0, 128.6, 128.2, 126.1, 122.0, 116.2, 96.5, 74.6, 30.3, 21.6, 20.5, 18.8, 13.3; MS *m/e* (relative intensity) 320 (M^+, 8), 278 (100), 105 (60). Anal. Calcd for $C_{21}H_{20}O_3$: C, 78.73; H, 6.29. Found: C, 79.01; H, 6.32.

***p*-Methyl-*o*-(phenylethynyl)phenol (9b):** mp 59−60 °C; IR 3520, 2180, 765, 690 cm^{-1}; ^1H NMR δ 7.49−6.83 (m, 8H), 5.95 (s, 1H), 2.22 (s, 3H); ^{13}C NMR 154.3, 131.7, 131.4, 131.0, 129.4, 128.5, 128.3, 122.4, 121.8, 114.5, 109.1, 95.6, 83.4; MS *m/e* (relative intensity) 208 (M^+, 100), 178 (34). Anal. Calcd for $C_{15}H_{12}O$: C, 86.51; H, 5.81. Found: C, 86.23; H, 5.78.

***o*-(Phenylethynyl)phenol (9c):** mp 47−48 °C; IR 3500, 2115, 820, 660 cm^{-1}; ^1H NMR δ 7.53−6.68 (m, 9H), 5.91 (bs, 1H); ^{13}C NMR 156.4, 131.6, 131.5, 130.4, 128.7, 128.4, 122.3, 120.4, 114.7, 109.5, 96.3, 83.0; MS *m/e* (relative intensity) 194 (M^+, 100), 165 (61). Anal. Calcd for $C_{14}H_{10}O$: C, 86.57; H, 5.19. Found: C, 86.29; H, 5.22.

***p*-Chloro-*o*-(phenylethynyl)phenol (9d):** mp 92−93 °C; IR 3400, 790, 730, 660 cm^{-1}; ^1H NMR δ 7.52−6.85 (m, 8H), 5.90 (bs, 1H); ^{13}C NMR 155.0, 131.5, 130.9, 130.3, 128.5, 128.4, 116.0, 97.1, 81.8; MS *m/e* (relative intensity) 230 (M^+, 25), 228 (M^+, 100), 165 (79). Anal. Calcd for $C_{14}H_9ClO$: C, 73.53; H, 3.97. Found: C, 73.77; H, 4.00.

***p*-Benzoyl-*o*-((17-acetylandrosta-3,5-dien-3-yl)ethynyl)-phenol (9e):** mp 84−87 °C; IR 3350, 2160, 1700, 1650, 1590, 780, 690 cm^{-1}; ^1H NMR δ 7.85−7.01 (m, 8H), 6.40 (s, 1H), 5.57 (bs, 1H), 2.04 (s, 3H), 0.95 (s, 3H), 0.85 (s, 3H); ^{13}C NMR δ 209.6, 194.4, 159.8, 141.0, 137.8, 136.7, 134.4, 132.0, 128.8, 127.4, 116.0, 110.4, 99.1, 81.9; MS *m/e* (relative intensity) 518 (M^+, 19), 105 (100). Anal. Calcd for $C_{36}H_{38}O_3$: C, 83.36; H, 7.38. Found: C, 83.59; H, 7.41.

***p*-Benzoyl-*o*-(hex-1-ynyl)phenol (9f):** oil; IR 3300, 1650, 770, 695 cm^{-1}; ^1H NMR δ 7.64−6.61 (m, 8H), 5.65 (bs, 1H), 2.45 (t, 2H), 1.59 (m, 4H), 0.94 (t, 3H); ^{13}C NMR 196.6, 161.4, 160.2, 132.2, 129.9, 128.8, 128.6,126.1, 127.4, 114.3, 110.5, 102.2, 30.5, 28.5, 22.1, 13.7; MS *m/e* (relative intensity) 278 (M^+, 80), 235 (100), 105 (50). Anal. Calcd for $C_{19}H_{18}O_2$: C, 81.99; H, 6.52. Found: C, 81.71; H, 6.49.

Typical Procedure for the Preparation of 2-Substituted-benzo[*b*]furans 7 from *o*-Ethynylphenols 3. Procedure A. 2-(Cholesta-3,5-dien-3-yl)benzo[*b*]furan (7a). To a stirred solution of *o*-ethynylphenol (**3a**) (0.174 g, 1.47 mmol) and Et_3N (4 mL) in DMF (4 mL) were added cholesta-3,5-dien-3-yl triflate (**6a**) (0.630 g, 1.22 mmol), $Pd(OAc)_2(PPh_3)_2$ (0.046 g, 0.06 mmol), and CuI (0.012 g, 0.06 mmol). The reaction mixture was stirred at 80 °C for 1 h under nitrogen. Diethyl ether and 0.1 N HCl were added, and the organic layer was separated, washed with water, dried (Na_2SO_4), and concentrated under reduced pressure. The residue purified by flash chromatography (silica gel, 97/3 v/v *n*-hexane/EtOAc) afforded **7a** (0.460 g, 78% yield): mp 210−212 °C; IR 2950, 1620, 1470,1450, 780, 740, 730 cm^{-1}; ^1H NMR δ 7.50−715 (m, 4H), 6.78 (s, 1H), 5.71 (bs, 1H); ^{13}C NMR δ 157.2, 154.6, 141.5, 129.3, 127.2, 126.6, 123.9, 125.5, 122.5, 120.4, 110.7, 101.1; MS *m/e* (relative intensity) 484 (M^+, 100), 131 (63). Anal. Calcd for $C_{35}H_{48}O$: C, 86.72; H, 9.98. Found: C, 86.99; H, 10.01.

2-(17β-(Benzoyloxy)androst-2-en-3-yl)benzo[*b*]furan (7b): mp 203−204 °C; IR 1710, 1260, 770, 725, 695 cm^{-1}; ^1H NMR δ 8.07−8.02 (m, 2H), 7.72−7.14 (m, 7H), 6.49 (s, 2H), 4.82 (t, 1H), 4.23 (m, 1H); ^{13}C NMR δ 166.5, 157.9, 154.4, 132.7, 128.5, 126.3, 122.5, 110.7, 100.1, 83.3; MS *m/e* (relative

intensity) 494 (M^+, 7), 105 (100). Anal. Calcd for $C_{34}H_{38}O_3$: C, 82.55; H, 7.74. Found: C, 82.28; H, 7.69.

2-(*β*-Naphthyl)benzo[*b*]furan (7c): mp 150−151 °C; IR 1600, 800, 780, 630, 615 cm^{-1}; ^1H NMR δ 8.36 (s, 1H), 7.93−7.23 (m, 10H), 7.12 (s, 1H); ^{13}C NMR δ 155.9, 155.0, 133.4, 133.2, 129.2, 128.4, 127.7, 126.6, 124.4, 123.6, 123.9, 122.7, 120.9, 111.1, 101.9; MS *m/e* (relative intensity) 244 (M^+, 100), 215 (33). Anal. Calcd for $C_{18}H_{12}O$: C, 88.50; H, 4.95. Found: C, 88.89; H, 4.92.

2-(4-Phenylcyclohex-1-enyl)-5-cyanobenzo[*b*]furan (7e): mp 168−170 °C; IR 2190, 790, 770, 720 cm^{-1}; ^1H NMR δ 7.60−7.22 (m, 8H), 6.75 (bs, 1H), 6.5 (s, 1H); ^{13}C NMR δ 159.2, 156.1, 146.0, 129.8, 128.5, 128.4, 127.6, 126.8, 126.3, 125.3, 111.7, 106.3, 99.9, 39.5, 33.5, 29.2, 25.4; MS *m/e* (relative intensity) 299 (M^+, 30), 195 (100), 104 (40). Anal. Calcd for $C_{21}H_{17}NO$: C, 84.25; H, 5.72; N, 4.68. Found: C, 83.91; H, 5.75; N, 4.71.

2-(2*H*-2-Phenylbenzopyran-4-yl)-5-methylbenzo[*b*]furan (7f): oil; IR 1590, 1570, 1340, 1320, 1280, 1190, 780, 730, 670 cm^{-1}; ^1H NMR δ 7.75−6.94 (m, 12H), 6.47 (d, J = 4 Hz, 1H), 6.36 (s, 1H), 5.66 (d, J = 4 Hz, 1H), 2.01 (s, 3H); ^{13}C NMR δ 160.6, 154.0, 132.3, 129.8, 128.7, 128.6, 128.4, 128.3, 127.2, 126.2, 125.3, 117.0, 110.6, 102.5, 96.6, 76.4, 21.3; MS *m/e* (relative intensity) 338 (M^+, 100), 261 (51). Anal. Calcd for $C_{24}H_{18}O_2$: C, 85.18; H, 5.36. Found: C, 85.45; H, 5.33.

2-(3-(Benzoyloxy)estra-1,3,5(10),16-tetraen-17-yl)-5-methylbenzo[*b*]furan (7g): mp 173−175 °C; IR 1740, 1620, 1370, 800, 720, 700 cm^{-1}; ^1H NMR δ 8.21−6.94 (m, 11H), 6.57 (s, 1H), 6.37 (bs, 1H), 2.91 (bs, 2H), 2.34 (s, 3H), 2.14−1.41 (m, 11H), 1.02 (s, 3H); ^{13}C NMR δ 166.0, 153.7, 153.3, 149.3, 145.1, 136.8, 132.5, 130.7, 129.8, 128.0, 126.7, 125.9, 122.2, 121.2, 119.3, 110.8, 102.1; MS *m/e* (relative intensity) 488 (M^+, 21), 105 (100). Anal. Calcd for $C_{34}H_{32}O_3$: C, 83.58; H, 6.60. Found: C, 83.29; H, 6.63.

Typical Procedure for the Preparation of *o*-Alkynylaryl Acetates 12 and 2-Substituted-benzo[*b*]furans 7 from *o*-((Trimethylsilyl)ethynyl)aryl Acetates 5. Procedure B. *o*-[(4-*tert*-Butylcyclohex-1-enyl)ethynyl]phenyl Acetate (12h) and 2-(4-*tert*-Butylcyclohex-1-enyl)benzo-[*b*]furans 7h. To a stirred solution of *o*-((trimethylsilyl)-ethynyl)phenyl acetate (**5a**) (0.244 g, 1.05 mmol) and Et_3N (0.78 mL) in THF (2 mL) were added 4-*tert*-butylcyclohex-1-enyl triflate (**6h**) (0.266 g, 0.93 mmol), $Pd(PPh_3)_4$ (0.021 g, 0.019 mmol), and tetrabutylammonium fluoride (1.0 M solution in THF, 1.12 mL). The reaction mixture was stirred at 60 °C for 5 h under nitrogen. Diethyl ether and 0.1 N HCl were added and the organic layer was separated, washed with water, dried (Na_2SO_4), and concentrated under reduced pressure. The residue, purified by flash chromatography (silica gel, 95/5 v/v *n*-hexane/EtOAc), afforded **12h** (0.166 g, 60% yield) [^1H NMR δ 7.47−7.02 (m, 4H), 6.18 (bs, 1 H) 2.30 (s, 3H), 2.28−2.26 (m, 3H), 2.25−2.22 (m, 2H), 1.82−1.22 (m, 2H), 0.97 (s, 9H); ^{13}C NMR δ 166.7, 151.3, 135.9, 132.7, 126.6, 125.8, 122.0, 120.3, 117.9, 96.0, 81.9, 43.1, 32.1, 30.6, 27.5, 27.0, 23.7, 20.8] and **7h** (0.026 g, 11% yield) [mp 65−67 °C; IR 3030, 1580, 1490, 1470, 1380, 1270, 810, 760, 740 cm^{-1}; ^1H NMR δ 7.49−7.14 (m, 4H), 6.58 (bs, 1H), 6.46 (s, 1H), 2.3−1.2 (m, 7H), 0.91 (s, 9H); ^{13}C δ 157.2, 154.4, 129.1, 126.3, 123.7, 122.4, 120.5, 120.4, 110.6, 100.1, 43.6, 32.2, 27.0, 26.4, 24.4, 22.8; MS *m/e* (relative intensity) 254 (M^+, 49), 170 (100). Anal. Calcd for $C_{18}H_{22}O$: C, 84.99; H, 8.72. Found: C, 84.65; H, 8.75].

After NMR characterization, **12h** was dissolved in MeOH (2 mL), piperidine (0.27 mL) was added, and the mixture was stirred for 3 h at 60 °C. Diethyl ether and 1 N HCl were added and, after workup, **7h** was obtained in 96% yield (0.137 g).

***o*-(5-Pyrimidylethynyl)phenyl Acetate (12g) and 2-(5-Pyrimidyl)benzo[*b*]furan (7d).** The palladium-catalyzed reaction of **5a** with 5-bromopyrimidine (**6d**) according to the same procedure described above led to the isolation of the coupling derivative **12g** (30% yield) [^1H NMR δ 9.54 (s, 1H), 9.04 (s, 2H), 7.53−6.82 (m, 4H), 2.28 (s, 3H); ^{13}C NMR δ 166.6, 158.4, 156.7, 133.0, 132.6, 131.2, 130.6, 126.0, 122.4, 120.2, 91.3, 86.6, 20.7] and of **7d** (15% yield) **7d**: mp 101−102 °C; IR 3100, 1470, 1450, 1410, 810, 740, 810, 740, 710 cm^{-1}; ^1H NMR δ 9.18 (s, 1H), 9.16 (s, 2H), 7.82−7.26 (m, 4H), 7.18 (s, 1H); ^{13}C NMR δ 157.7, 152.2, 152.7, 146.6, 137.7, 131.3, 126.2, 125.8, 125.6, 124.9, 123.5, 121.5, 121.4, 111.4, 104.2; MS *m/e* (relative intensity) 196 (M^+, 100), 142 (43), 114 (30). Anal. Calcd for $C_{12}H_8N_2O$: C, 73.46; H, 4.11; N, 14.28. Found: C, 73.17; H, 4.13; N, 14.33].

After NMR characterization, **12g** was treated with methanol and piperidine to give the corresponding benzo[*b*]furan **7d** in 95% yield.

2,3-Bis(5-pyrimidyl)benzo[*b*]furan (8d): mp 231−234 °C; IR 1600, 1560, 1550, 1270, 720, 710, 700 cm^{-1}; ^1H NMR δ 9.35 (b, 1H), 9.20 (b, 1H), 8.96 (b, 2H), 7.66−7.27 (m, 4H); ^{13}C NMR δ 158.5, 157.1, 154.3, 128.3, 126.9, 124.6, 124.1, 119.1, 111.9; MS *m/e* (relative intensity) 274 (M^+, 100), 246 (11), 166 (33). Anal. Calcd for $C_{16}H_{10}N_4O$: C, 70.07; H, 3.67; N, 20.43. Found: C, 70.31; H, 3.68; N, 20.51.

2,3-Bis(4-(carboxymethyl)phenyl)benzo[*b*]furan (8j): mp 174−177 °C; IR 1725, 1610, 1285, 845, 770, 740 cm^{-1}; ^1H NMR δ 8.15 (AA′ part of an AA′BB′ system, J = 8.5 Hz, 2H), 7.94 (AA′ part of an AA′BB′ system, J = 8.7 Hz, 2H), 7.66 (BB′ part of an AA′BB′ system , J = 8.7 Hz, 2H), 7.53 (BB′ part of an AA′BB′ system, J = 8,5, 2H), 3.97 (s, 3H), 3.90 (s, 3H); ^{13}C NMR δ 166.3, 154.1, 149.6, 139.2, 129.6, 126.6, 125.5, 124.4, 123.0, 119.9, 103.3, 52.1, 52.0; MS *m/e* (relative intensity) 386 (M^+, 100), 355 (26), 268 (42). Anal. Calcd for $C_{24}H_{18}O_5$: C, 74.60; H, 4.70. Found: C, 74.91; H, 4.67.

Typical Procedure for the Preparation of 2-Substituted-benzo[*b*]furans 7 from *o*-((Trimethylsilyl)ethynyl)-aryl Acetates 5. Procedure C. 5-Methyl-2-(*m*-(trifluoromethyl)phenyl)benzo[*b*]furan (7l). To a stirred solution of *p*-methyl-*o*-((trimethylsilyl)ethynyl)phenyl acetate (**5b**) (0.490 g, 1.99 mmol) and *m*-(trifluoromethyl)phenyl iodide (**6l**) (1.890 g, 2.39 mmol) in anhydrous 1-methyl-2-pyrrolidinone (8 mL) were added potassium *tert*-butoxide (0.490 g, 4.38 mol) and $Pd(PPh_3)_4$ (0.046 g, 0.04 mmol). The reaction mixture was stirred at 70 °C for 1 h under nitrogen. Diethyl ether and 0.1 N HCl were added, and the organic layer was separated, neutralized with a saturated $NaHCO_3$ solution, washed with water, dried (Na_2SO_4), and concentrated under reduced pressure. The residue purified by flash chromatography (silica gel, *n*-hexane) afforded **7l** (0.297 g, 54% yield): mp 101−103 °C; IR 1590, 1310, 1260, 1000, 790, 780 cm^{-1}; ^1H NMR δ 8.02−7.07 (m, 7H), 6.67 (s, 1H), 2.36 (s, 3H); ^{13}C NMR δ 154.1, 153.4, 127.7, 126.2, 124.5, 110.7, 102.3, 21.2; MS *m/e* (relative intensity) 276 (M^+, 100), 207 (6), 178 (18). Anal. Calcd for $C_{16}H_{11}F_3O$: C, 69.56; H, 4.01. Found: C, 69.70; H, 4.04.

2-(4-(Methoxycarbonyl)phenyl)benzo[*b*]furan (7i): mp 164−166 °C; IR 1730, 1620, 1280, 805, 770, 750 cm^{-1}; ^1H NMR δ 8.09 (AA′ part of an AA′BB′ system, J = 10 Hz, 2H), 7.55 (BB′ part of an AA′BB′ system, J = 10 Hz, 2H), 7.34−7.29 (m, 4H), 7.11 (s, 1H), 3.96 (s, 3H); ^{13}C NMR δ 166.6, 155.1, 154.5, 129.5, 124.6, 111.3, 103.4, 52.1; MS *m/e* (relative intensity) 252 (M^+, 100), 221 (70), 165 (54). Anal. Calcd for $C_{16}H_{12}O_3$: C, 76.18; H, 4.79. Found: C, 76.51; H, 4.76.

2-(4-Methoxyphenyl)benzo[*b*]furan (7j): mp 145−147 °C; IR 1615, 1245, 835, 790, 740, 730 cm^{-1}; ^1H NMR δ 7.80−7.75 (AA′ part of an AA′BB′ system, J = 11.8 Hz, 2H), 7.56−7.19 (m, 4H), 6.99−6.93 (BB′ part of an AA′BB′ system, J = 11.8 Hz, 2H), 6.86 (s, 1H), 3.82 (s, 3H); ^{13}C NMR δ 138.2, 129.5, 126.4, 126.3, 123.7, 123.3, 120.2, 116.4, 114.3, 120.2, 116.4, 114.3, 114.2, 111.0, 99.7, 55.3; MS *m/e* (relative intensity) 224 (M^+, 100), 209 (32). Anal. Calcd for $C_{15}H_{12}O_2$: C, 80.34; H, 5.39. Found: C, 80.15; H, 5.42.

5-Methyl-2-(*p*-chlorophenyl)benzo[*b*]furan (7k): mp 178−180 °C; IR 1590, 1265, 870, 830, 815, 800 cm^{-1}; ^1H NMR δ 7.77−7.07 (m, 7H), 6.91 (s, 1H), 2.43 (s, 3H); ^{13}C NMR δ 154.3, 153.3, 129.0, 126.4, 120.8, 110.7, 101.5, 21.4; MS *m/e* (relative intensity) 244 (M^+, 32), 242 (M^+, 100), 178 (30). Anal. Calcd for $C_{15}H_{11}ClO$: C, 74.23; H, 4.57. Found: C, 74.49; H, 4.54.

Typical Procedure for the Preparation of 2,3-Disubstituted-benzo[*b*]furans 14. Procedure D. 2-Phenyl-3-(3,3,5,5-tetramethylcyclohex-1-enyl)-5-benzoylbenzo[*b*]-furan (14c). To a stirred solution of *o*-phenylethynylphenol (**9c**) (0.130 g, 0.67 mmol) in MeCN (5 mL) were added 3,3,5,5-tetramethylcyclohex-1-enyl triflate (**6n**) (0.192 g, 0.67 mmol), KOAc (0.328 g, 3.35 mmol), and $Pd(PPh_3)_4$ (0.039 g, 0.033 mmol). The reaction mixture was stirred at 45 °C for 4 h under nitrogen. EtOAc and a $NaHCO_3$ saturated solution were

added and the organic layer was separated, washed with water, dried (Na_2SO_4), and concentrated under reduced pressure. The residue purified by flash chromatography (silica gel, 95/5 v/v *n*-hexane/EtOAc afforded **14c** (0.174 g, 60% yield): oil; IR 1660, 1250, 760, 680 cm^{-1}; ^1H NMR δ 8.01−7.37 (m, 13H), 5.71 (s, 1H), 2.03 (s, 2H), 1.45 (s, 2H), 1.06 (s, 6H), 1.04 (s, 6H); ^{13}C NMR δ 196.8, 156.7, 151.7, 139.1, 138.7, 132.8, 130.8, 129.0, 128.9, 127.4, 125.4, 120.1, 111.3, 48.9, 42.4, 33.6, 31.6, 30.4; MS *m/e* (relative intensity) 434 (M^+, 32), 419 (30), 105 (100). Anal. Calcd for $C_{31}H_{30}O_2$: C, 85.68; H, 6.96. Found: C, 85.89; H, 6.94.

2-Phenyl-3-(17*β*-acetylandrosta-3,5-dien-3-yl)benzo[*b*]furan (14a): mp 221−224 °C; IR 1720, 1250, 870, 830 cm^{-1}; ^1H NMR δ 7.84−6.28 (m, 9H), 5.99 (s, 1H), 5.52 (b, 1H), 2.12 (s, 3H), 1.12 (s, 3H), 0.85 (s, 3H); ^{13}C NMR δ 208.6, 153.9, 150.1, 141.5, 131.2, 128.4, 127.3, 126.7, 124.4, 11.0, 63.7, 57.1, 48.1, 44.1, 31.8, 21.1, 19.3, 13.4; MS *m/e* (relative intensity) 490 (M^+, 100). Anal. Calcd for $C_{35}H_{38}O_2$: C, 85.67; H, 7.81. Found: C, 85.89; H, 7.84.

2-Phenyl-3-(17*β*-acetylandrosta-3,5-dien-3-yl)-5-benzoylbenzo[*b*]furan (14b): mp 235−237 °C; IR 1700, 1640, 1280, 890, 810, 740, 700, 680 cm^{-1}; ^1H NMR δ 8.08−7.40 (m, 13H), 6.35 (s, 1H), 5.50 (b, 1H), 2.13 (s, 3H), 1.08 (s, 3H), 0.68 (s, 3H); ^{13}C NMR δ 208.5, 195.5, 155.2, 140.1, 137.1, 131.6, 130.2, 129.0, 126.6, 127.5, 126.2, 125.8, 109.5, 62.6, 56.0, 47.0, 43.1, 37.7, 33.6, 30.7, 18.2, 12.3; MS *m/e* (relative intensity) 594 (M^+, 19), 105 (100). Anal. Calcd for $C_{42}H_{42}O_3$: C, 84.81; H, 7.12. Found: C, 84.53; H, 7.09.

2-(17*β*-Acetylandrosta-3,5-dien-3-yl)-3-(3,3,5,5-tetramethylcyclohex-1-enyl)-5-benzoylbenzo[*b*]furan (14d): mp 99−100 °C; IR 1715, 1665, 715 cm^{-1}; ^1H NMR δ 7.92−7.42 (m, 8H), 6.68 (s, 1H), 5.62 (bs 1H), 5.59 (s, 1H), 2.03 (s, 3H), 1.17 (s, 6H), 1.08 (s, 6H), 1.05 (s, 3H), 0.67 (s, 3H); ^{13}C NMR δ 209.5, 196.4, 155.9, 152.9, 141.5, 138.3, 132.1, 130.4, 128.8, 128.0, 126.8, 126.6, 126.4, 124.9, 123.1, 119.0, 110.4; MS *m/e* (relative intensity) 654 (M^+, 4), 105 (100). Anal. Calcd for $C_{46}H_{54}O_3$: C, 84.36; H, 8.31. Found: C, 84.67; H, 8.28.

2-Phenyl-3-(*β*-naphthyl)-5-benzoylbenzo[*b*]furan (14e): mp 125−126 °C; IR 1670, 780, 700, 690 cm^{-1}; ^{13}C NMR δ 196.5, 157.5, 157.1, 138.2, 132.9, 132.1, 128.9, 128.0, 126.8, 126.2, 125.0, 124.0, 111.0, 101.5; MS *m/e* (relative intensity) 424 (M^+, 3), 298 (79), 221 (100), 105 (51). Anal. Calcd for $C_{31}H_{20}O_2$: C, 87.71; H, 4.75. Found: C, 87.45; H, 4.73.

Typical Procedure for the Preparation of 3-Acyl-2-substituted-benzo[*b*]furan 15. Procedure E. 2-Phenyl-3-(3,3,5,5-tetramethylcyclohex-1-enecarbonyl)-5-benzoylbenzo[*b*]furan (15c). To a stirred solution of *o*-(phenylethynyl)-*p*-benzoylphenol (**9a**) (0.200 g, 0.67 mmol) in MeCN (5 mL) were added 3,3,5,5-tetramethylcyclohex-1-enyl triflate (**6n**) (0.190 g, 0.67 mmol), KOAc (0.328 g, 3.35 mmol), and Pd(PPh_3)$_4$ (0.039 g, 0.033 mmol). The flask was purged with carbon monoxide for few seconds and connected to a balloon of carbon monoxide. The reaction mixture was stirred at 45 °C overnight and poured into a separatory funnel containing a saturated $NaHCO_3$ solution and ethyl acetate. The organic layer was separated, and the aqueous layer was extracted twice with ethyl acetate. The combined organic layers were dried (Na_2SO_4) and evaporated under vacuum. The residue was purified by flash chromatography on silica gel eluting with a 90/10 v/v *n*-hexane/EtOAc mixture to give 0.196 g (64% yield) of **15c**: mp 99−101 °C; IR 1665, 1650 cm^{-1}; ^1H NMR δ 8.16−7.06 (m, 13H), 6.23 (s, 1H), 2.19 (bs, 2H), 1.23 (s, 2H), 0.93 (s, 6H), 0.65 (s, 6H); ^{13}C NMR δ 196.3, 193.3, 157.5, 156.1, 153.3, 137.9, 135.5, 133.6, 132.6, 129.9, 129.0, 128.8, 128.5, 128.3, 127.5, 126.8, 125.0, 124.0, 116.3, 111.2, 101.5, 49.1, 36.5, 30.1, 29.7; MS *m/e* (relative intensity) 462 (M^+, 17), 105 (100). Anal. Calcd for $C_{32}H_{30}O_3$: C, 83.09; H, 6.54. Found: C, 83.36; H, 6.52.

2-Phenyl-3-(*β*-naphthoyl)-5-benzoylbenzo[*b*]furan (15a): mp 120−124 °C; IR 1660, 1640, 760, 730, 690 cm^{-1}; ^{13}C NMR δ 195.8, 191.5, 158.5, 155.8, 137.5, 134.6, 133.5, 132.3, 130.1, 120.6, 128.8, 128.4, 128.3, 128.2, 127.7, 127.6, 124.7, 116,4, 11.5; MS *m/e* (relative intensity) 452 (M^+, 19), 325 (17), 127 (100), 105 (55). Anal. Calcd for $C_{32}H_{20}O_3$: C, 84.94; H, 4.45. Found: C, 84.60; H, 4.47.

2-Phenyl-3-(17*β*-acetylandrosta-3,5-diene-3-carbonyl)-5-benzoylbenzo[*b*]furan (15b): mp 178- 182 °C ; IR 1715, 1670, 1630, 720, 690 cm^{-1}; ^1H NMR δ 8.05−7.38 (m, 3H), 6.70 (s, 1H), 5.29 (bs, 1H), 2.12 (s, 3H), 0.77 (s, 3H), 0.63 (s, 3H); ^{13}C NMR δ 209.3, 196.2, 192.5, 155.9, 143.9, 141.6, 137.9, 134.6, 134.1, 133.5, 132.2, 131.2, 130.0, 129.7, 128.6, 128.2, 127.8, 111.2, 110.6; MS *m/e* (relative intensity) 622 (M^+, 10), 325 (100). Anal. Calcd for $C_{43}H_{42}O_4$: C, 82.93; H, 6.80. Found: C, 82.61; H, 6.83.

2-Phenyl-3-(4-*tert*-butylcyclohex-1-enecarbonyl)-5-benzoylbenzo[*b*]furan (15d): oil; IR 1680, 1660 cm^{-1}; ^1H NMR δ 8.06−7.25 (m, 13H), 6.70 (bs, 1H), 2.40−2.38 (m, 1H), 1.98−1.60 (m, 4H), 1.25−0.89 (m, 2H), 0.83 (s, 9H); ^{13}C NMR δ 196.3, 192.9, 156.8, 155.8, 140.5, 139.3, 132.3, 130.0, 129.8, 128.6, 128.3, 128.1, 127.8, 124.0, 111.2, 43.3, 32.0, 27.9, 27.0, 23.2, 20.0; MS *m/e* (relative intensity) 462 (M^+, 14), 405 (12), 325 (18), 105 (100). Anal. Calcd for $C_{32}H_{30}O_3$: C, 83.09; H, 6.54. Found: C, 83.31; H, 6.51.

2-Phenyl-3-(3,3,5,5-tetramethylcyclohex-1-enecarbonyl)-5-chlorobenzo[*b*]furan (15e): mp 95−96 °C; IR 1645, 790, 760, 680 cm^{-1}; ^1H NMR δ 7.71−728 (m, 3H), 6.25 (s, 1H), 2.21 (s, 2H), 1.33 (s, 2H), 0.98 (s, 6H), 0.65 (s, 6H); ^{13}C NMR δ 193.3, 157.5, 153.1, 135.4, 129.9, 129.3, 128.6, 128.5, 126.4, 125.4, 123.7, 115.6, 49.1, 36.5, 33.5, 29.7, 29.6; MS *m/e* (relative intensity) 394 (M^+, 17), 392 (M^+, 50), 257 (33), 255 (100). Anal. Calcd for $C_{25}H_{25}ClO_2$: C, 76.42; H, 6.41. Found: C, 76.11; H, 6.43.

***o*-Phenylethynyl-*p*-chloro-(*m*-(trifluoromethyl)benzoyloxy)benzene (16a):** mp 55−56 °C; IR 1750, 1250, 740, 680 cm^{-1}; ^1H NMR δ 8.54−7.16 (m,12H); ^{13}C NMR δ 152.4, 133.5, 133.4, 132.4, 131.5, 130.4, 129.4, 129.0, 128.4, 126.0, 123.4, 122.0, 121.2, 115.0, 112.3, 95.8, 82.6; MS *m/e* (relative intensity) 402 (M^+, 9), 400 (M^+, 28), 173 (100). Anal. Calcd for $C_{22}H_{12}ClF_3O_2$: C, 65.93; H, 3.02. Found: C, 65.80; H, 3.00.

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