Palladium-Catalyzed Carbonylative Annulation of *o*-Alkynylphenols: Syntheses of 2-Substituted-3-aroyl-benzo[*b*]furans

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Abstract: We report here a general synthetic methodology for palladium-catalyzed carbonylative annulation of *o*-alkynylphenol to construct 2-substituted-3-aroyl-benzo[*b*]furan. On the basis of the results, this methodology could be applied to a wider selection of iodide substrates to generate desired products. In accordance with mechanistic studies, this process involves coordination of cationic and less hindered acyl palladium complexes with *o*-alkynylphenols to create a desired cascade triad (coordination, nucleophilic addition, and reductive elimination). Consistent with this mechanism, addition of 1 equiv of $AgBF_4$ to palladium catalyst $Pd(Ph_3P)_4$ generates an ideal candidate for this unique transformation.

The search for new methodologies that allow rapid construction of polycyclic scaffolds in a single operation is a fertile field of research, especially for combinatorial chemistry.[1] In this area, recent advances in palladium-catalyzed carbonylative annulation of *o*-alkynylphenols to synthesize the scaffold of benzo[*b*]furans have emerged as extremely valuable tools in the design of consecutive cyclization processes (Figure 1).[2]

Aroyl-benzo[*b*]furans serve as core structures of many naturally occurring products and pharmaceutical drug candidates.[3] Some 3-aroyl-benzo[*b*]furans as well as their derived molecules such as compounds **I**−**III** (Figure 2), have shown unusual biological activities.[4]

The scaffold of 2-substituted-3-aroyl-benzo[*b*]furans **2** could be constructed directly by palladium-catalyzed carbonylative annulation of *o*-alkynylphenols **1** with various iodobenzenes (corresponding to R″X in Figure 1). This approach is particularly attractive since this synthetic transformation will allow us to combine the generation of one carbon−heteroatom bond in the benzo[*b*]furan's ring with the formation of two carbon−carbon bonds at the C-3 position.

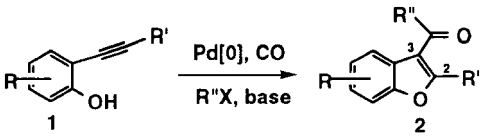


Figure 1. General synthetic scheme for palladium-catalyzed carbonylative heteroannulation.

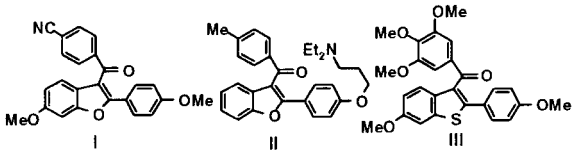
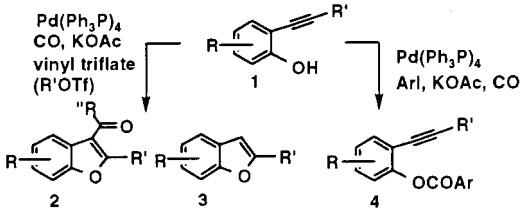


Figure 2. Biologically active molecules.

Scheme 1. Palladium-Catalyzed Carbonylative Annulation of *o*-Alkynylphenols



Although this approach is promising, as far as we are aware, there have been very few reports related to this synthetic transformation. Recently, Arcadi reported the direct formation of 2-substituted-3-aroyl-benzo[*b*]furans **2** from the *σ*-acylpalladium-catalyzed carbonylative annulation of *o*-alkynylphenol **1**.[5] In his study, the product **2** was generated in 20−60% yield from vinyl triflate and *o*-alkynylphenols **1**, together with the direct cyclization product **3** (Scheme 1). However, when vinyl triflate was replaced with aryl iodide, the ester **4** was obtained as the sole product

Our long-standing interests in construction of a benzofuran library encouraged us to develop highly efficient methods for diversification of a benzofuran scaffold for combinatorial syntheses.[6]

We initiated our investigation by using *o*-alkynylphenol **5**[6a] as a substrate to evaluate the carbonylative annulation reaction. Thus, the five commercially available aryliodides were selected as electrophiles to generate the corresponding *σ*-acylpalladium complex **B** (see Figure 3). To our surprise, *o*-alkynylphenol **5** was converted to the corresponding phenol ester **6** in high yield in all cases, together with a small amount of direct cyclization product **7**, and no 3-aroyl-benzo[*b*]furans were detected (Scheme 2).

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(1) (a) Posner, G. H. *Chem. Rev.* **1986**, *86*, 831−844. (b) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49−92. (c) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115−136. (d) Negishi, E.-I.; Copéret, C.; Ma, S. M.; Liou, S.-Y.; Liu, F. *Chem. Rev.* **1996**, *96*, 365−393. (e) Ojima, I.; Tzamarioudaki, M.; Li, Z. Y.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635−662. (f) Thompson, L. A.; Ellman, J. A. *Chem Rev.* **1996**, *96*, 555−600.

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(5) Arcadi, A.; Cacchi, S.; Del Rosario, M.; Fabrizi, G.; Marinelli, F. *J. Org. Chem.* **1996**, *61*, 9280.

(6) (a) Nan, Y.; Miao, H.; Yang, Z. *Org. Lett.* **2000**, *2*, 297. (b) Liao, Y.; Fathi, R.; Reitman, M.; Zhang, Y.; Yang, Z. *Tetrahedron Lett.* **2001**, *42*, 1815−1818. (c) Hu, Y.-H.; Yang, Z. *Org. Lett.* **2001**, *3*, 1387−1390.

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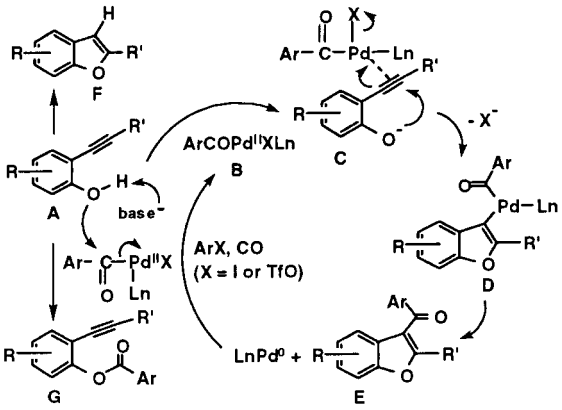
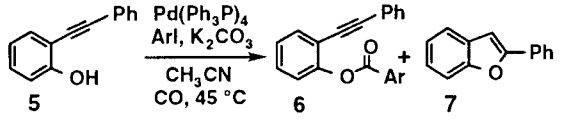


Figure 3. Proposed mechanism of *σ*-acylpalladium-catalyzed carbonylative annulation of *o*-alkynylphenols.

Scheme 2. Esterification of *o*-Alkynylphenol 5



We therefore, directed our attention to determining the inherent factors, which could regulate the reaction to follow different paths.

Mechanistically, the *σ*-acylpalladium complex catalyzed carbonylative annulation of *o*-alkynylphenols leading to the anticipated 3-aroyl-benzo[*b*]furans might proceed via the multistage process shown in Figure 3.[7]

The overall process for this catalytic cycle might involve (1) coordination of the *σ*-acylpalladium **B** (ArCOPd^{II}XLn) to *o*-alkynylphenol **A** to generate the complex **C**; (2) nucleophilic addition of the phenolic oxide to the ArCOPd^{II}XLn-activated arylacetylene **C** to form intermediate **D**; (3) reductive elimination of **D** to produce 3-aroyl-benzo[*b*]furan **E** and generate the palladium(0) at the same time; and (4) reoxidation of the palladium(0), followed by insertion of CO to ArCOPd^{II}X **B** to complete the cycle.

However, there are two other approaches that can also compete with the above cycle by base-promoted direct cyclization (from **A** to **F**) and intermolecular attack of the phenolic oxide to the *σ*-acylpalladium complex **B** (ArCOPd^{II}XLn) to give the phenol ester (from **A** to **G**).

We inferred that the coordination between the *σ*-acylpalladium **B** and *o*-alkynylphenols is paramount to the success of generating the desired product **E**, since a failure of this coordination would lead to either direct generation of the benzo[*b*]furan **F** or formation of phenyl ester **G** (Figure 3). As our projected target molecules are 2,3-disubstituted benzo[*b*]furans, we had to use the internal acetylenes as substrates; as a result, the *σ*-acylpalladium species should be either cationic or sterically less hindered in order to allow efficient coordination between the *σ*-acylpalladium **B** and *o*-alkynylphenol.

Recent investigations have indicated that cationic palladium complexes exhibit high reactivity toward coordination of alkenes or alkynes to bring about efficient carbonylation reactions,[8] and such cationic complexes can be easily prepared by reaction of silver salts of BF_4^-, ClO_4^-, and BAr_4^- with organopalladium halides in the presence of tertiary phosphine ligands or chelating diamine (diimine) ligands.[8b−f]

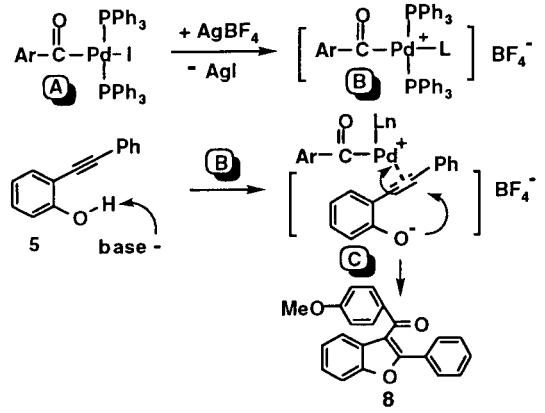
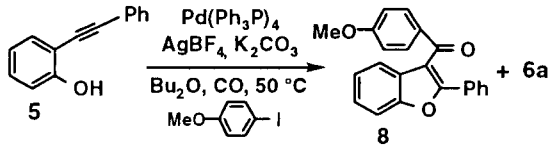


Figure 4. Cationic palladium complex catalyzed carbonylative annulation of *o*-alkynylphenol **5**.

Scheme 3. Synthesis of 2-Phenyl-3-aroyl-benzo[*b*]furan 8



We believed that these complexes would be more efficient for coordination with internal acetylenes, and the newly generated cationic palladium acetylene complexes might efficiently promote carbonylative annulation of *o*-alkynylphenols.

After screening a number of different palladium catalysts with an equal amount of $AgBF_4$ under carbonylative annulation conditions, we found that *o*-alkynylphenol **5** can be cyclocarbonylated to form **8** in a 30% yield under a balloon pressure of CO at 50 °C in dibutyl ether with a catalytic amount of the cationic complex (5 mol %) generated by reaction of $Pd(PPh_3)_4$ with $AgBF_4$. Under this procedure, only a trace amount of phenyl ester **6a** was observed (Scheme 3).

We considered that the complex **B** generated from the organopalladium iodide **A** contains a cationic metal center with Lewis acid character and has a tendency to coordinate the unsaturated triple bond to form the complex **C**, which eventually leads to the product **8** (Figure 4).

Encouraged by the above results, we started to search for sterically less hindered catalysts. We found that $Pd_2(dpa)_3$/bpy[8e] (5 mol %) catalyzes the carbonylative annulation of *o*-alkynylphenol **5** to generate a 40% yield of compound **8** together with a 27% yield of **6a**.

We next directed our attention to testing substituted *o*-alkynylphenols as substrates for this reaction, since the substitution groups on the *o*-alkynylphenols might yield better results than the unsubstituted substrates on the basis of our previous experiences in synthesizing other benzo[*b*]furan molecules.

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(8) (a) Ali, B. E.; Okuro, K.; Vasapollo, G.; Alper, H. *J. Am. Chem. Soc.* **1996**, *118*, 4264. (b) Lapointe, A. M.; Brookhart, M. *Organometallics* **1998**, *17*, 1530. (c) Lim, N.-K.; Yaccato, K. J.; Dghaym, R. D.; Arndtsen, B. A. *Organometallics* **1999**, *18*, 3953. (d) Reddy, K. R.; Chen, C.-L.; Liu, Y.-H.; Peng, S.-M.; Chen, J.-T.; Liu, S.-T. *Organometallics* **1999**, *18*, 2574. (e) Yagyu, T.; Osakada, K.; Brookhart, M. *Organometallics* **2000**, *19*, 2125. (f) Kisanga, P.; Goj, L. A.; Widenhoefer, R. A. *J. Org. Chem.* **2001**, *66*, 635.

Scheme 4. Synthesis of Substituted 2-Phenyl-3-aroyl-benzo[*b*]furan 10

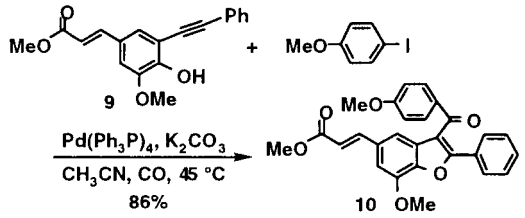
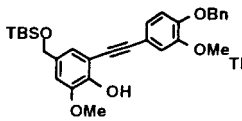
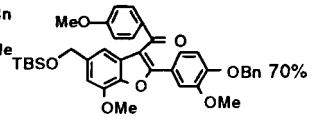
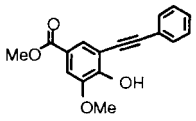
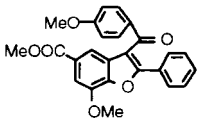
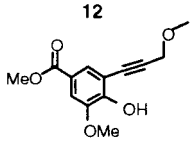
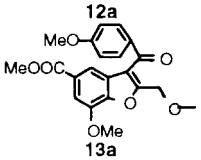


Table 1. Palladium-Catalyzed Carbonylative Annulation of *o*-Alkynylphenols with 4-Iodoanisole

Entry	*o*-Alkynylphenols	Product	Yield[a]
1	 11	 11a	70%
2	 12	 12a	72%
3	 13	 13a	90%

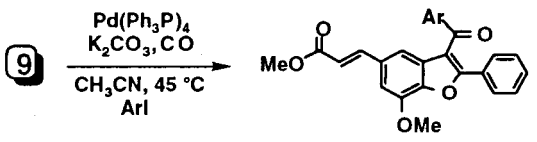
For this purpose, compound **9**[6a] was used to optimize the reaction conditions with the various σ-acylpalladium complexes **B** generated from 4-iodoanisole and palladium catalysts such as $PdCl_2$, $PdCl_2(PPh_3)_2$, $Pd(OAc)_2$, PdI_2, and PdI_2−thiourea[6a] as well as $Pd(PPh_3)_4$−$AgBF_4$[8d] with bases (including Et_2NH, Et_3N, Cs_2CO_3, CsOAc, Na_2CO_3, and NaOAc) in solvents (e.g., benzene, DMF, THF, ether, acetonitrile, and dioxane) under the cabonylative reaction conditions. It was interesting to find that a simple combination of 4-iodoanisole, $Pd(Ph_3P)_4$, and K_2CO_3 in acetonitrile at 45 °C under a balloon pressure of CO (ca. 5 psi) gave the best results among all the other combinations, and the desired product **10** was obtained in an 86% yield (Scheme 4).

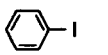
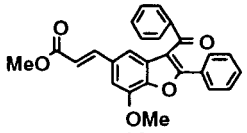
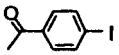
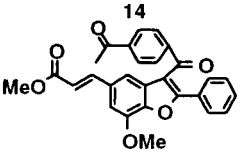
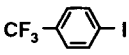
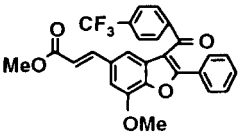
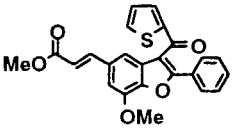
We therefore, investigated the generality of the reaction. Toward this end, three *o*-alkynylphenols **11**−**13** were prepared by Sonogashira couplings of iodophenol acetates with the corresponding terminal acetylenes, followed by removal of the acetyl group. They were annulated under conditions identical to those described above. As we expected, satisfactory results were obtained for these cyclizations, which are summarized in Table 1.

Finally, we evaluated the effect of substituents on the aryliodide for this palladium-catalyzed annulation reaction. The reaction conditions chosen were those used for the synthesis of the 3-aroyl-benzo[*b*]furans listed in Scheme 4 for comparison purposes, and compound **9** was once again selected as a substrate for this reaction. The results are summarized in Table 2.

According to these results, phenyl iodides substituted with electron-donating groups (entry 1) gave better yields than products with electron-withdrawing groups (entries 2 and 3). Even 2-iodothiophene (entry 4) gave a reasonable yield of product, which suggested that other heterocyclic iodides might also participate in this type of annulation.

Table 2. Palladium-Catalyzed Carbonylative Annulation of *o*-Alkynylphenol 9 with Different Substituted Phenyl Iodides



Entry	Iodide	Prodcut	Yield[a]
1		 14	91%
2		 15	61%
3		 16	45%
4		 17	68%

In summary, we have developed a highly efficient synthetic approach for the carbonylative cyclization of *o*-alkynylphenols to the corresponding 2-substituted-3-aroyl-benzo[*b*]furans under mild conditions. Importantly, the ability to manipulate multiple steps (one carbon−heteroatom bond and two carbon−carbon bonds) in this carbonylative annulation process will make this method a powerful tool for the combinatorial synthesis of these types of molecules on solid supports, which is currently under investigation.

Experimental Section

General Methods. Unless stated otherwise, all reactions were performed in flame-dried glassware under nitrogen or an argon atmosphere. Reaction solvents were commercially purchased from Aldrich without further purification and reagents were used as received. Reactions were monitored by thin-layer chromatography (TLC) on 0.25 mm precoated Merck Silica Gel 60 F_{254}, visualizing with ultraviolet light, *p*-anisaldehyde stain, or phosphomolybdic acid stain. Flash column chromatography was performed on Merck Silica Gel 60 (230−400 mesh) using reagent-grade hexanes, dichloromethane, and ACS-grade ethyl acetate, methanol, and diethyl ether. High-resolution mass spectra were performed at Harvard University Mass Spectrometry. ^1H and ^{13}C NMR spectra were recorded on a Varian Unity INPVA 500 MHz spectrometer. ^1H−^1H couplings are assumed to be first order, and peak multiplicity is reported as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), or b (broad).

General Procedure for Synthesis of α-Alkynylphenols. A mixture of phenyl iodide A (0.2 mmol), acetylene B (0.3 mmol), copper(I) iodide (0.02 mmol), and dichlorobis-(triphenylphosphine)palladium (0.01 mmol) in dry acetonitrile (40 mL) was degassed with argon for 10 min. The reaction mixture was treated with triethylamine (280 μL, 2.0 mmol) and stirred at 25 °C for 24 h. The reaction mixture was concentrated, and the residue was purified by flash column chromatography to afford

the coupling product. The coupling product was treated with $NH_3 \cdot H_2O$ (0.5 mL) in a solvent of THF and MeOH (1:1, 10 mL) at 25 °C for 30 min, followed by concentration, and the residue was purified by flash column chromatography to give the pure product.

Compound 9: 98% yield as a white solid; ^{1}H NMR δ 7.61 (d, J = 16.0 Hz, 1H), 7.57−7.59 (m, 2H), 7.37−7.38 (m, 3H), 7.28 (d, J = 2.0 Hz, 1H), 7.02 (d, J = 2.0 Hz, 1H), 6.34 (d, J = 16.0 Hz, 1H), 6.25 (s, 1H), 3.96 (s, 3H), 3.82 (s, 3H); ^{13}C NMR δ 167.3, 148.5, 146.8, 144.0, 131.6, 128.5, 128.2, 126.5, 125.6, 122.6, 116.0, 110.1, 109.6, 94.8, 83.3, 56.1, 51.5; MS (APCI) [$C_{19}H_{16}O_4$], m/z (M^+) calcd 308, found 308.

Compound 12: 90% yield as a white solid; ^{1}H NMR δ 7.85 (d, J = 2.0 Hz, 1H), 7.57−7.59 (m, 2H), 7.53 (d, J = 2.0 Hz, 1H), 7.35−7.37 (m, 3H), 6.49 (s, 1H), 3.96 (s, 3H), 3.92 (s, 3H); ^{13}C NMR δ 166.2, 150.5, 146.3, 131.6, 128.5, 128.2, 127.1, 122.7, 121.9, 111.8, 109.6, 94.7, 83.3, 56.2, 52.0; MS (APCI) [$C_{17}H_{14}O_4$], m/z (M^+) calcd 282, found 282.

Others are known compounds (see ref 6a).

Two Different Methods for the Synthesis of Compound 8: Method 1. To a mixture of compound **5** (0.15 mmol), aromatic iodide (0.30 mmol), K_2CO_3 (0.75 mmol), $AgBF_4$ (0.15 mmol), and $Pd(PPh_3)_4$ (0.0075 mmol) in a dry round-bottom flask (25 mL) was added dry butyl ether (4 mL) by cannulation. The reaction mixture was degassed for 10 min with CO and then stirred at 50 °C under a balloon pressure of CO for 4 h. The reaction mixture was cooled, filtered through a pad of silica gel, and washed by EtOAc. The filtrate was concentrated, and the residue was purified by flash chromatography (8/1 toluene/EtOAc) to give **8** in 30% yield. **Method 2.** A mixture of $Pd_2(dpa)_3$ (0.0075 mmol), 2,2′-bipyridine (0.015 mmol), and aromatic iodide (0.30 mmol) in benzene was stirred for 3 h at 50 °C under N_2. To this solution was added compound **5** in acetonitrile (2 mL), followed by K_2CO_3 (0.75 mmol). The reaction mixture was degassed for 10 min with CO and then stirred at 50 °C under a balloon pressure of CO for 12 h. The reaction mixture was cooled, filtered through a pad of silica gel, and then washed with EtOAc. The filtrate was concentrated, and the residue was purified by flash chromatography (8/1 toluene/EtOAc) to give **8** in 40% yield and **6a** in 27% yield.

Compound 8: ^{1}H NMR δ 7.78 (d, J = 8.5 Hz, 2H), 7.73 (m, 2H), 7.59 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 7.0 Hz, 1H), 7.36 (m, 1H), 7.32−7.34 (m, 3H), 7.25 (t, J = 7.0 Hz, 1H), 6.84 (d, J = 8.5 Hz, 1H), 3.84 (s, 3H); ^{13}C NMR δ 191.2, 164.1, 156.5, 154.0, 132.6, 130.8, 129.0, 128.7, 128.3, 125.5, 123.9, 121.6, 116.6, 114.0, 55.7; HRMS (EI) [$C_{22}H_{16}O_3$], m/z (M^+) calcd 328.1100, found 328.1093.

General Procedure for Synthesis of 2-Substituted-3-aroyl-benzo[*b*]furans. To a mixture of *o*-alkynylphenol (1 mmol), aromatic iodide (2 mmol), K_2CO_3 (5 mmol), and $Pd(PPh_3)_4$ (0.05 mmol) in a dry round-bottom flask (25 mL) was added dry acetonitrile (10 mL) by cannulation. The reaction mixture was degassed for 10 min with CO and then stirred at 45 °C under a CO balloon for 5 h. The reaction mixture was cooled, filtered through a pad of silica gel, and then washed with EtOAc. The filtrate was concentrated, and the residue was purified by flash chromatography to give the pure product.

Compound 10: 86% yield as a white solid; ^{1}H NMR δ 7.87 (d, J = 9.0 Hz, 2H), 7.73−7.74 (m, 2H), 7.70 (d, J = 16.0 Hz, 1H), 7.33−7.34 (m, 3H), 7.26 (s, 1H), 7.04 (s, 1H), 6.85 (d, J = 9.0 Hz, 2H), 6.39 (d, J = 16.0 Hz, 1H), 4.10 (s, 3H), 3.85 (s, 3H), 3.81 (s, 3H); ^{13}C NMR δ 190.3, 167.3, 163.9, 157.0, 145.3, 145.0, 144.3, 132.2, 131.1, 130.6, 130.1, 129.7, 128.9, 128.4, 128.0, 117.0, 116.4, 114.5, 113.7, 106.1, 56.2, 55.5, 51.3; HRMS(EI) [$C_{27}H_{22}O_6$], m/z (M^+) calcd 442.1416, found: 442.1407.

Compound 11a: 70% yield as a white solid; ^{1}H NMR δ 7.87 (d, J = 9.0 Hz, 2H), 7.36−7.42 (m, 6H), 7.31 (d, J = 7.0 Hz, 1H), 7.27 (s, 1H), 7.02 (s, 1H), 6.91 (s, 1H), 6.84 (d, J = 9.0 Hz, 2H), 5.15 (s, 2H), 4.77 (s, 2H), 4.06 (s, 3H), 3.83 (s, 3H), 3.77 (s, 3H), 0.93 (s, 9H), 0.09 (s, 6H); ^{13}C NMR δ 191.1, 163.9, 157.0, 149.5, 149.4, 145.0, 142.3, 138.3, 136.8, 132.4, 130.9, 130.4, 128.7, 128.1, 127.4, 122.9, 121.4, 115.8, 113.9, 113.5, 112.0, 110.7, 105.9, 71.0, 65.3, 56.2, 56.1, 55.6, 26.1, 18.5, −5.1; HRMS (ES) [$C_{38}H_{42}O_7$-Si], m/z (M^+ + 1) calcd 639.2778, found 639.2734.

Compound 12a: 72% yield as a white solid; ^{1}H NMR δ 7.89 (s, 1H), 7.87 (d, J = 9.0 Hz, 2H), 7.72−7.74 (m, 2H), 7.60 (s, 1H), 7.31−7.34 (m, 3H), 6.84 (d, J = 9.0 Hz, 2H), 4.12 (s, 3H), 3.91 (s, 3H), 3,84 (s, 3H); ^{13}C NMR (125.7 MHz) δ 190.3, 167.1, 164.2, 157.1, 145.9, 145.2, 132.5, 130.2, 130.0, 129.1, 128.7, 128.2, 127.0, 116.9, 116.1, 114.0, 108.4, 56.5, 55.6, 52.3; HRMS (ES) [$C_{25}H_{20}O_6$], m/z (M^+ + 1) calcd 417.1338, found 417.1313.

Compound 13a: 90% yield as a white solid; ^{1}H NMR δ 7.92 (d, J = 9.0 Hz, 2H), 7.87 (s, 1H), 7.58 (s, 1H), 6.99 (d, J = 9.0 Hz, 2H), 4.60 (s, 3H), 4.09 (s, 3H), 3.92 (s, 3H), 3.91 (s, 2H), 3.40 (s, 3H); ^{13}C NMR δ 188.7, 166.7, 163.9, 158.1, 146.0, 144.9, 131.9, 130.7, 127.8, 126.8, 120.0, 116.4, 113.8, 108.1, 65.2, 58.7, 56.1, 55.4, 52.1; HRMS (ES) [$C_{21}H_{20}O_7$], m/z (M^+ + 1) calcd 385.1287, found 385.1267.

Compound 14: 91% yield as a white solid; ^{1}H NMR δ 7.83 (d, J = 8.0 Hz, 2H), 7.70 (d, J = 16.0 Hz, 1H), 7.68 (m, 2H), 7.50 (t, J = 7.5 Hz, 1H), 7.28−7.36 (m, 6H), 7.04 (s, 1H), 6.39 (d, J = 16.0 Hz, 1H), 4.10 (s, 3H), 3.81 (s, 3H); ^{13}C NMR δ 191.7, 167.2, 158.4, 145.3, 145.0, 144.3, 137.3, 133.2, 131.3, 130.3, 129.8, 129.6, 128.8, 128.3, 128.2, 117.1, 116.1, 114.6, 106.1, 56.1, 51.5; HRMS (ES) [$C_{26}H_{20}O_5$], m/z (M^+ + 1) calcd 413.1389, found 413.1401.

Compound 15: 61% yield as a white solid; ^{1}H NMR δ 7.87 (s, 4H), 7.72 (d, J = 15.5 Hz, 1H), 7.63 (d, J = 7.0 Hz, 2H), 7.39 (s, 1H), 7.26−7.33 (m, 3H), 7.07 (s, 1H), 6.41 (d, J = 15.5 Hz, 1H), 4.10 (s, 3H), 3.81 (s, 3H), 2.60 (s, 3H); ^{13}C NMR δ 197.2, 190.9, 167.2, 159.4, 145.4, 144.9, 144.5, 140.8, 139.9, 131.6, 130.5, 130.2, 129.9, 129.8, 128.6, 128.3, 128.1, 117.4, 115.9, 114.6, 106.3, 56.1, 51.6, 26.7; HRMS (ES) [$C_{28}H_{23}O_6$], m/z (M^++1) calcd 455.1495, found: 455.1505.

Compound 16: 45% yield as a white solid; ^{1}H NMR δ 7.88 (d, J = 8.0 Hz, 2H), 7.73 (d, J = 16.0 Hz, 1H), 7.57 (m, 4H), 7.45 (s, 1H), 7.26−7.34 (m, 3H), 7.08 (s, 1H), 6.43 (d, J = 16.0 Hz, 1H), 4.10 (s, 3H), 3.82 (s, 3H); ^{13}C NMR δ 190.5, 167.2, 159.7, 145.4, 144.8, 144.5, 140.3, 131.8, 130.2, 129.8, 128.7, 128.5, 128.4, 128.3, 128.2, 125.3, 125.2, 117.4, 115.7, 114.5, 106.4, 56.1, 51.6; HRMS (ES) [$C_{27}H_{19}F_3O_5$], m/z (M^+ + 1) calcd 481.1263, found 481.1238.

Compound 17: 68% yield as a white solid; ^{1}H NMR δ 7.78 (m, 2H), 7.72 (d, J = 16.0 Hz, 1H), 7.68 (dd, J = 4.0, 1.0 Hz, 1H), 7.45 (dd, J = 4.0, 1.0 Hz, 1H), 7.39 (s, 1H), 7.35−7.39 (m, 3H), 7.04 (s, 1H), 6.96 (dd, J = 4.0 Hz, 1H), 6.41 (d, J = 16.0 Hz, 1H), 4.09 (s, 3H), 3.81 (s, 3H); ^{13}C NMR δ 183.2, 167.2, 157.1, 145.3, 144.9, 144.3, 143.9, 135.1, 135.0, 131.3, 130.1, 129.9, 128.8, 128.4, 128.1, 128.0, 117.2, 116.3, 114.2, 106.2, 56.1, 51.5; HRMS (ES) [$C_{24}H_{18}O_5S$], m/z (M^+ + 1) calcd 419.0953, found 419.0966.

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Supporting Information Available: Experimental procedures and ^{1}H and ^{13}C NMR spectra for all new compounds This material is available free of charge via the Internet at http://pubs.acs.org.

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