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COMMUNICATION

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A Regio- and Stereoselective Carbonylative Approach to Alkyl (*Z*)-2-[3-Oxoisobenzofuran-1-(3*H*)-ylidene]acetates

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Abstract. The first example of the oxidative carbonylation of 2-ethynylbenzoic acid derivatives, leading to alkyl (*Z*)-2-[3-oxoisobenzofuran-1-(3*H*)-ylidene]acetates in a regio- and stereoselective manner, is reported. Under the catalytic action of PdI_2 (2 mol%) in conjuction with KI (20 mol%), different 2-[(trimethylsilyl)ethynyl]benzoic acids were converted into the corresponding isobenzofuranones in high to excellent yields (70-98%). The proposed reaction mechanism involves *syn* 5-*exo*-dig cyclization, carbon monoxide insertion, and nucleophilic displacement by an alcohol. Desilylation occurred under the reaction conditions. The structure of a representative product, that is, methyl (*Z*)-2-[3-oxoisobenzofuran-1(3*H*)-ylidene]acetate, was confirmed by XRD analysis.

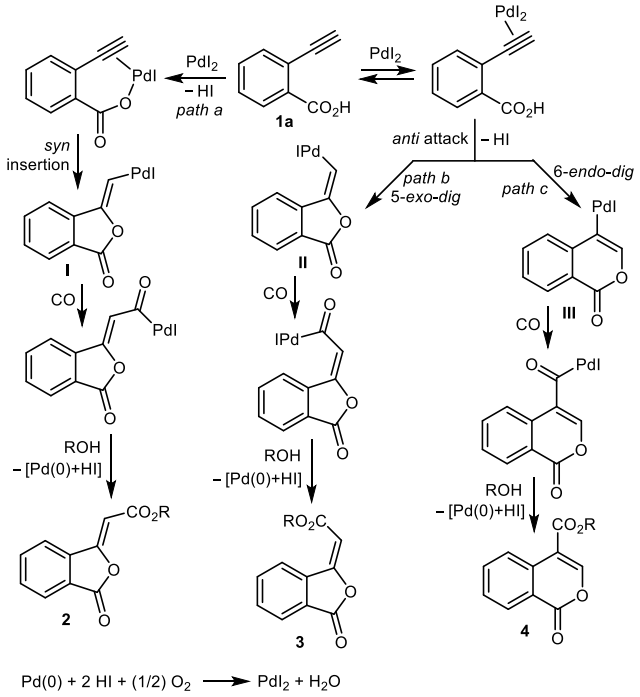
Keywords: carbonylation; cyclization; 2-ethynylbenzoic acids; isobenzofuranones; palladium

Palladium-catalyzed carbonylative heterocyclization of suitably substituted acetylenic substrates, carried out under oxidative conditions, is one of the most important methods for the synthesis of carbonylated heterocycles.[1] Numerous examples of this approach have been reported in the literature with *ortho*-functionalized arylacetylenes as starting materials.[1,2] However, to the best of our knowledge, the direct use of readily available 2-alkynylbenzoic acids has not been reported so far in this kind of process.[3] This is probably due to the low nucleophilicity of the free carboxylic group associated with its coordinating ability, which may cause catalyst deactivation.

In this Communication, we wish to fill this gap, by reporting our preliminary results on the direct oxidative carbonylation of 2-ethynylbenzoic acid derivatives leading to alkyl (*Z*)-2-[3-oxoisobenzofuran-1-(3*H*)-ylidene]acetates. The process is carried out using a very simple catalytic system (PdI_2 in conjunction with an excess of KI) under relatively mild conditions (80 °C and under 40 atm of a 4:1 mixture of CO-air, in a dioxane-ROH medium, R = alkyl).[4]

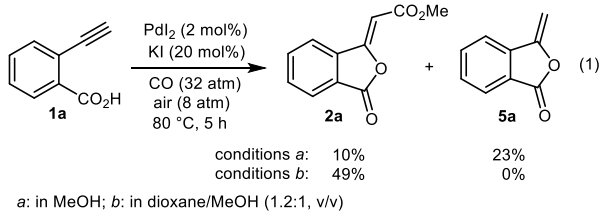
We started our investigation with simple 2-ethynylbenzoic acid **1a**. In principle, different reaction pathways could be followed when allowing to react **1a** under PdI_2-catalyzed oxidative carbonylation conditions, carried out in the presence of O_2 as oxidant and ROH as nucleophile (Scheme 1; anionic iodide ligands are omitted for clarity). A first possibility corresponds to the formation of a palladium carboxylate intermediate **I** from the reaction between **1a** and PdI_2, with elimination of HI (Scheme 1, pathway *a*). Stereospecific carbon monoxide insertion, followed by nucleophilic displacement by ROH, would then lead to the final alkyl (*Z*)-2-[3-oxoisobenzofuran-1-(3*H*)-ylidene]acetate **2** with *Z* stereochemistry. Another possible pathway would involve an initial *anti* intramolecular nucleophilic attack of the carboxylic group to the triple bond coordinated to the metal center, a kind of reactivity that has often been observed with nucleophilic groups different from carboxylate.[1,5] Either 5-*exo-dig* (Scheme 1, *pathway b*) or 6-*endo-dig* (Scheme 1, *pathway c*) cyclization may take place, with formation of the corresponding regiosomeric vinylpalladium complexes **II** and **III**. Alkoxycarbonylation of the latter would then lead to the final regioisomeric heterocyclic derivatives (**3** and **4**, respectively). In any case, Pd(0) would be formed,

which would then be reoxidized by the action of oxygen.



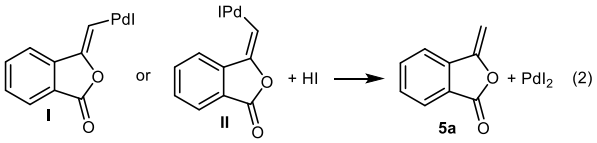
Scheme 1. Possible divergent pathways in the PdI_2-catalyzed oxidative cyclization-alkoxycarbonylation of 2-ethynylbenzoic acid **1a**.

The first experiment carried out with **1a** was performed under the following reaction conditions: 2 mol % of PdI_2, 20 mol % of KI, at 80 °C in MeOH as the solvent (**1a** concentration: 0.05 mmol per mL of MeOH) and under 40 atm of a 4:1 mixture of CO-air. After 5 h, analysis of the reaction crude showed the formation of a mixture of cyclized products, that are, methyl (*Z*)-2-[3-oxoisobenzofuran-1-(3*H*)-ylidene]acetate **2a** (10% yield) and 3-methyleneisobenzofuranone **5a** (23% yield) (Equation 1). The structure of **2a**, including the *Z* configuration, was confirmed by XRD analysis (see Figure 1 and the Supporting Information for details).



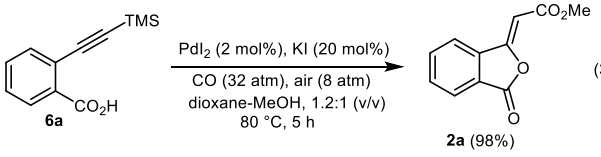
Formation of **2a**, with *Z* stereochemistry, was clearly in agreement with pathway *a* of Scheme 1, while **5a** corresponded to protonolysis of either intermediate **I** or **II** (Equation 2).

Figure 1. Molecular structure of methyl (*Z*)-2-(3-oxoisobenzofuran-1(3*H*)-ylidene)acetate **2a** showing the atom-labeling scheme. See Supporting Information for details.



We then tried to improve the selectivity toward the carbonylated product **2a** by changing several reaction parameters. In particular, to minimize the protonolysis by-reaction leading to non-carbonylated **5a** (Equation 2), an experiment was carried out in a less protic medium, that is, a dioxane/MeOH mixture (1.2:1, v/v). In fact, it is known from the literature that protonolysis may be favored by a protic medium.[6] In agreement with this hypothesis, the reaction carried out in the dioxane/MeOH mixture turned out to be selective toward the formation of **2a**, obtained in 49% yield, with no formation of **5a** (Equation 1). The variation of other parameters, such as the substrate concentration or the reaction temperature, did not lead to a significant improvement of this result in terms of yield and selectivity of **2a** (data not shown).

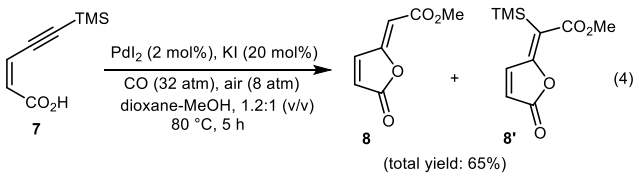
A dramatic augment of the **2a** yield was instead observed when the oxidative carbonylation reaction was carried out on 2-[(trimethylsilyl)ethynyl]benzoic acid **6a**, bearing the trimethylsilyl group on the triple bond (Equation 3). In this case, in fact, the oxidative carbonylation, carried out in dioxane-MeOH (1.2:1, v/v) as the solvent, selectively afforded the desilylated carbonylated isobenzofuranone derivative **2a** in almost quantitative yield (98%) (Equation 3 and Table 1, entry 1).[7,8]



The process also worked nicely when employing a lower catalyst loading, even though the **2a** yield decreased to some extent: with 1, 0.33, and 0.2 mol% of PdI_2, the **2a** yields were 75, 69, and 58% respectively (Table 1, entry 1). Thus, with 0.2 mol% catalyst, a turnover number (TON) as high as 290 mmol of **2a** per mmol of palladium employed was obtained.

Other differently substituted substrates **6b-d**, bearing on the aromatic ring either an electron-withdrawing group (Cl, Table 1, entries 2) or a π-donating group (Me or OMe, Table 1, entry 3 and 4, respectively), were then tested. Under the same conditions employed for **6a** (Table 1, entry 1), substrates **6b-d** afforded the corresponding alkyl (*Z*)-2-[3-oxoisobenzofuran-1-(3*H*)-ylidene]acetates **2b-d** in high to excellent yields (70-95%; Table 1, entries 2-4). Very good results were also obtained using different alcohols as nucleophiles, such as EtOH (**2e** yield, 90%; Table 1, entry 5), or *i*-PrOH (**2f** yield, 93%: Table 1, entry 6). A remarkable yield of 74% of isobenzofuranone **2g** was observed even with a sterically demanding alcohol, such as *t*-BuOH (Table 1, entry 7).

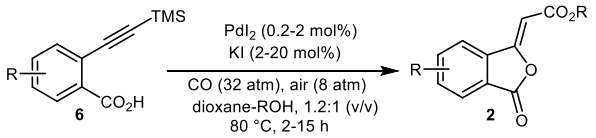
We also tested the reactivity of (*Z*)-5-(trimethylsilyl)pent-2-en-4-ynoic acid **7** under the optimized conditions.[9] As shown in Equation 4, this substrate was converted into a mixture of desilylated and silylated carbonylation products (**8** and **8'**, respectively) in 65% total yield.[10]

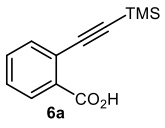
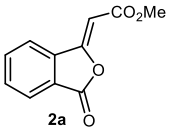
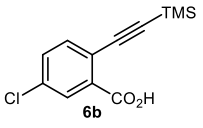
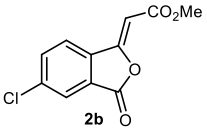
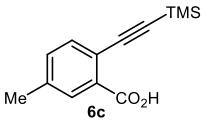
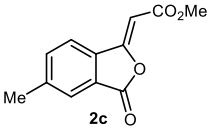
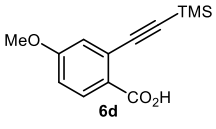
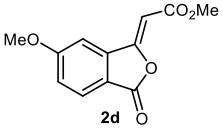
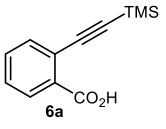
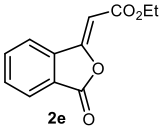
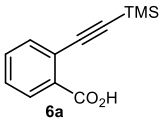
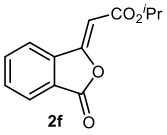
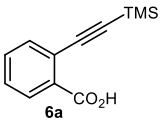
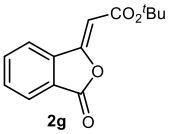


(4)

In conclusion, we have reported the first example of the oxidative carbonylation of 2-ethynylbenzoic acid derivatives **1** and **6**, carried out with PdI_2 in conjunction with KI as catalyst under relatively mild reaction conditions (80 °C under 40 atm of a 4:1 mixture of CO-air) to give alkyl (*Z*)-2-[3-oxoisobenzofuran-1-(3*H*)-ylidene]acetates **2** in a regio- and stereoselective manner. The process works much better, in terms of product yield and catalytic efficiency, starting directly from substrates **6**, bearing the triple bond substituted with the TMS group (70-98% yields of **2** and turnover numbers up to 290 mmol of product per mmol of palladium were achieved). This is a clear practical advantage, considering that 2-[(trimethylsilyl)ethynyl]benzoic acids **6** are synthetic precursors of unprotected 2-ethynylbenzoic acids **1**. The method disclosed here therefore represents a valuable novel entry to an important class of heterocyclic derivatives,[11] starting from simple and readily available substrates (2-[(trimethylsilyl)ethynyl]benzoic acids, CO, ROH, and O_2).

Table 1. Regio- and stereoselective synthesis of alkyl (*Z*)-2-[3-oxoisobenzofuran-1-(3*H*)-ylidene]acetates **2** by PdI_2/KI-catalyzed oxidative cyclization-alkoxycarbonylation of 2-[(trimethylsilyl)ethynyl]benzoic acids **6**.[a]



Entry	6	2	Yield [%][b]
1			98 75[c] 69[d] 58[e]
2[f]			80
3			70
4			95
5			90
6			93
7			74

[a] Unless otherwise noted, all reactions were carried out with in a dioxane-MeOH mixture (1.2:1, v/v) (substrate concentration: 0.02 mmol of substrate **6** per mL of solvent) at 80 °C under 40 atm (at 25 °C) of a 4:1 mixture of CO-air, in the presence of PdI_2 (2 mol%) and KI (20 mol%) for 5 h.

[b] Isolated yield based on starting **6**.

[c] The reaction was carried out with 1 mol % of PdI_2 and 10 mol % of KI.

[d] The reaction was carried out with 0.33 mol % of PdI_2 and 3.3 mol % of KI for 15 h.

[e] The reaction was carried out with 0.2 mol % of PdI_2 and 2 mol % of KI for 15 h.

[f] The reaction was carried out for 2 h.

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Experimental Section

General Methods

Solvents and chemicals were reagent grade and used without further purification. All reactions were analyzed by TLC on silica gel 60 F254 (Merck) and by GLC (Shimadzu GC-2010) using capillary columns with polymethylsilicone +5% phenylsilicone as the stationary phase (HP-5). Column chromatography was performed on silica gel 60 (Merck, 70−230 mesh). Evaporation refers to the removal of solvent under reduced pressure. Melting points are uncorrected. IR spectra were taken with a JASCO FTIR 4200 spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded at 25 °C on a 300 MHz spectrometer (Bruker DPX Avance 300) in $CDCl_3$ solutions with Me_4Si as the internal standard. Chemical shifts (δ) and coupling constants (J) are given in ppm and Hz, respectively. Mass spectra were obtained using a GC-MS apparatus (Shimadzu QP-2010) at 70 eV ionization voltage or an HPLC/ESI/Q- TOF HRMS apparatus; HPLC conditions were as follows: water, acetonitrile, and formic acid were of HPLC/MS grade; the HPLC system was an Agilent 1260 Infinity; a reversed- phase C18 column (ZORBAX Extended- C18 2.1 × 50 mm, 1.8 µm) with a Phenomenex C18 security guard column (4 mm × 3 mm) were used; the flow- rate was 0.4 mL/min and the column temperature was set to 30 °C; the eluents were formic acid–water (0.1:99.9, *v*/*v*) (phase A) and formic acid–acetonitrile (0.1:99.9, *v*/*v*) (phase B); the following gradient was employed: 0–10 min, linear gradient from 5% to 95% B; 10–15 min, washing and reconditioning of the column to 5% B; injection volume was 10 µL; the eluate was monitored through MS TIC. The mass spectra were recorded using an Agilent 6540 UHD accurate- mass Q- TOF spectrometer equipped with a Dual AJS ESI source working in negative mode, under the following conditions: N_2 was employed as desolvation gas at 300 °C and a flow rate of 9 L/min; the nebulizer was set to 45 psig; the sheath gas temperature was set at 400 °C and a flow of 12 L/min; a potential of 2.7 kV was used on the capillary for positive ion mode; the fragmentor was set to 175 V; the MS spectrum was recorded in the 150–1000 *m*/*z* range.

Preparation of Substrates

Substrates **1a**, **6a-d**, and **7** were prepared as described in the Supporting Information.

General Procedure for the Oxidative Carbonylation of 2-[(Trimethylsilyl)ethynyl]benzoic Acids 6 (Table 1)

A 250 mL stainless steel autoclave was charged in the presence of air with PdI_2 (2.2 mg, 6.1 × 10^{-3} mmol), KI (10.1 mg, 6.1 × 10^{-2} mmol) and a solution or **6** (0.30 mmol; **6a**, 65.6 mg; **6b**, 76.3 mg; **6c**, 70.5 mg; **6d**, 75.1 mg) in a mixture of dioxane (8.2 mL) and ROH (6.8 mL; R = Me, Et, *i*-Pr, *t*-Bu). The autoclave was sealed and, while the mixture was stirred, the autoclave was pressurized with CO (32 atm) and air (up to 40 atm). After being stirred at 80°C for the required time (5 h for **6a** with MeOH, EtOH, *i*-PrOH, *t*-BuOH, 5 h for **6c** and **6d** with MeOH, 2 h for **6b** with MeOH, see Table 1), the autoclave was cooled, degassed and opened. The solvent was evaporated, and the products were purified by column chromatography on silica gel using as eluent hexane to hexane/AcOEt 98:2.

Methyl (*Z*)-2-[3-oxoisobenzofuran-1-(3*H*)-ylidene]acetate (2a). Yield: 60.3 mg, starting from 65.6 mg of 2-[2-(trimethylsilyl)ethynyl]benzoic acid **6a** (98%). White solid, mp = 92-93°C. IR (KBr): ν = 1806 (s), 1719 (s), 1653 (s), 1588 (w), 1460 (w), 1435 (m), 1381 (m), 1244 (s), 1209 (m), 1148 (w), 1036 (s), 974 (m), 849 (m), 776 (m), 690 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.05 (d, J = 8.0, 1 H, aromatic), 7.96 (d, 1 H, J = 7.6, 1 H, aromatic), 7.83 (td, J = 7.6, 1.0, 1 H, aromatic), 7.71 (dd, J = 7.5, 0.7, 1 H, aromatic), 6.16 (s, 1 H, =CH), 3.84 (s, 3H, CO_2Me); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.0, 165.7, 158.0, 136.1, 135.3, 132.6, 128.2, 126.7, 125.4, 102.0, 51.9; GC/MS: *m*/*z* = 204 [M$^+$, 35], 173 (100), 163 (5), 146 (15), 133 (4), 104 (7), 89 (36); HRMS-ESI (*m*/*z*): [(M+H)$^+$] calcd for ($C_{11}H_9O_4$): 205.0495; found, 205.0493. The spectroscopic data were in good agreement with those reported.[12] CCDC 841258 contains the supplementary crystallographic data for this compound. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Methyl (*Z*)-2-[5-chloro-3-oxoisobenzofuran-1-(3*H*)-ylidene]acetate (2b). Yield: 57.4 mg, starting from 76.3 mg of 5-chloro-2-[(trimethylsilyl)ethynyl]benzoic acid **6b** (80%). White solid, mp = 96-98 °C. IR (KBr): ν = 1795 (s), 1712 (s), 1659 (s), 1465 (w), 1239 (s), 1163 (s), 1055 (s), 984 (w), 869 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.02 (d, br, J = 8.5,1 H, aromatic), 7.92 (s, br, 1 H, aromatic), 7.76 (dd, J = 8.5, 1.8, 1 H, aromatic), 6.17 (s, 1 H, =CH), 3.85 (s, 3 H, CO_2Me); ^{13}C NMR (75 MHz, $CDCl_3$): δ =165.9, 164.4, 157.2, 139.1, 135.5, 134.3, 129.5, 128.2, 125.3, 102.5, 52.1; GC/MS: *m*/*z* = 240 [(M+2)$^+$, 13], 238 [M$^+$, 38], 209 (33), 207 (100), 180 (14), 151 (4), 123 (37), 110 (10); HRMS-ESI (*m*/*z*): [(M+H)$^+$] calcd for ($C_{11}H_9ClO_4$): 239.0106; found, 239.0111.

Methyl (*Z*)-2-(5-Methyl-3-oxoisobenzofuran-1-(3*H*)-ylidene]acetate (2c). Yield: 46.1 mg, starting from 70.5 mg of 5-(methyl)-2-[(trimethylsilyl)ethynyl]benzoic acid **6c** (70%). White solid, mp = 108-109 °C. IR (KBr): ν = 1798 (s), 1717 (s), 1659 (s), 1435 (w), 1385 (w), 1250 (m), 1215 (m), 1165 (w), 1092 (w), 1057 (s), 984 (m), 841 (s), 706 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.90 (d, J = 8.1, 1 H aromatic), 7.75 (s, 1 H, aromatic), 7.62 (d, J = 8.1, 1 H, aromatic), 6.09 (s, 1 H, =CH), 3.83 (s, 3 H, CO_2Me), 2.53 (s, 3 H, Me); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.2, 165.8, 158.3, 143.8, 136.4, 133.7, 128.0, 126.9, 125.5, 101.0, 51.9, 21.7; GC/MS: *m*/*z* = 218 [M$^+$, 39], 187 (100), 160 (18), 147 (6), 103 (48), 77 (20); HRMS-ESI (*m*/*z*): [(M+H)$^+$] calcd for ($C_{12}H_{11}O_4$): 219.0652; found, 219.0653.

Methyl (*Z*)-2-[6-methoxy-3-oxoisobenzofuran-1-(3*H*)-ylidene]acetate (2d). Yield: 67.2 mg, starting from 75.1 mg of 4-methoxy-2-[(trimethylsilyl)ethynyl]benzoic acid **6d** (95%). White solid, mp = 169-170. °C. IR (KBr): ν = 1793 (s), 1712 (s), 1653 (s), 1600 (s), 1492 (m), 1445 (w), 1260 (s), 1200 (s), 1150 (w), 1044 (m), 860 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.63 (s, br, 1 H, aromatic), 7.84 (d, J = 8.5, 1 H, aromatic), 7.19 (d, br, J = 7.4, 1 H, aromatic), 6.11 (s, 1 H, =CH), 3.98 (s, 3 H, OMe), 3.83 (s, 3 H, CO_2Me); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.1, 165.6, 165.3, 158.1, 138.6, 126.7, 120.7, 118.7, 111.1, 101.8, 56.1, 52.0; GC/MS: *m*/*z* = 234 [M$^+$, 60], 203 (100), 176 (25), 163 (5), 147 (18), 119 (33); HRMS-ESI (*m*/*z*): [(M+H)$^+$] calcd for ($C_{12}H_{11}O_5$): 235.0601; found, 235.0595.

Ethyl (*Z*)-2-[3-oxoisobenzofuran-1-(3*H*)-ylidene]acetate (2e). Yield: 59.0 mg, starting from 65.4 mg of 2-[2-(trimethylsilyl)ethynyl]benzoic acid **6a** (90%). White solid, mp = 45-46 °C. IR (KBr): ν = 1788 (s), 1712 (s), 1654 (s) 1471 (w), 1359 (m), 1242 (s), 1200 (m), 1145 (m), 1046 (s), 861 (m), 774 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.05 (d, J = 7.9, 1 H, aromatic), 7.98-7.93 (m, 1 H, aromatic), 7.82 (td, J = 7.5, 1.1, 1 H, aromatic), 7.71 (td, J = 7.5, 0.9, 1 H, aromatic), 6.14 (s, 1 H, =CH), 4.30 (q, 2 H, J = 7.1, 2 H, CH_2CH$_3$), 1.37 (t, J = 7.1, 3 H, CH$_2$CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ =165.7, 165.5. 157.8, 136.1, 135.3, 132.5, 128.2, 126.5, 125.3, 102.5, 60.9, 14.3; GC/MS: *m*/*z* = 218 (M$^+$, 18), 190 (24), 173 (100), 146 (66), 118 (5), 105 (17), 89 (46), 76 (17); HRMS-ESI (*m*/*z*): [(M+H)$^+$] calcd for ($C_{12}H_{11}O_4$): 219.0652; found, 219.0648. The spectroscopic data were in good agreement with those reported.[13]

Isopropyl (*Z*)-2-[3-oxoisobenzofuran-1-(3*H*)-ylidene]acetate (2f). Yield: 64.9 mg, starting from 65.3 mg of 2-[2-(trimethylsilyl)ethynyl]benzoic acid **6a** (93%). White solid, mp = 57-58 °C. IR (KBr): ν = 1791 (s), 1710 (s), 1652 (s), 1589 (w), 1469 (m), 1377 (m), 1243 (s), 1142 (m), 1105 (m), 1027 (m), 972 (m), 833 (m), 774 (m), cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 9.06 (d, br, J = 7.9, 1 H, aromatic), 7.99-7.93 (m, 1 H, aromatic), 7.82 (td, J = 7.7, 1.1, 1 H, aromatic), 7.70 (td, J = 7.5, 0.9, 1 H aromatic), 6.12 (s, 1 H, =CH), 5.16 (hept, J = 6.2, 1 H, C*H*Me_2), 1.34 [d, J = 6.2, 6H, CH(CH_3)$_2$]; ^{13}C NMR (75 MHz, $CDCl_3$): δ =165.8, 165.1, 157.6, 136.2, 135.2, 132.4, 128.2, 126.5, 125.3, 103.0, 68.5, 21.9; GC/MS: m/z =232 [M^+, 8], 191 (12), 173 (94), 146 (100), 105 (27), 89 (46), 76 (17); HRMS-ESI (m/z): [$(M+H)^+$] calcd for ($C_{13}H_{13}O_4$): 233.0808; found, 233.0802.

***tert*-Butyl (*Z*)-2-[3-oxoisobenzofuran-1-(3*H*)-ylidene]acetate (2g)**. Yield: 55.0 mg, starting from 65.6 mg of 2-[2-(trimethylsilyl)ethynyl]benzoic acid **6a** (74%). White solid, mp = 73-74 °C. IR (KBr): ν = 1800 (s), 1717 (m), 1650 (s), 1472 (w), 1366 (m), 1252 (s), 1140 (m), 1028 (s), 972 (w), 847 (m), 788 (m), 687 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ =9.03 (d, J = 7.9, 1 H, aromatic), 7.95 (d, J = 7.5, 1 H, aromatic), 7.81 (t, J = 7.5, 1 H aromatico), 7.69 (t, J = 7.5, 1 H, aromatic), 6.09 (s, 1 H, =CH), 1.57 (s, 9 H, *t*-Bu); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.9, 164.8, 157.0, 136.3, 135.2, 132.2, 128.2, 126.5, 125.2, 104.5, 81.5, 28.2; GC/MS: m/z = 246 [M^+, 3], 191 (76), 173 (100), 162 (11), 149 (22), 146 (52), 105 (30), 89 (37), 57 (48); HRMS-ESI (m/z): [$(M+Na)^+$] calcd for ($C_{14}H_{14}NaO_4$): 269.0784; found, 269.0779.

Oxidative Carbonylation of (*Z*)-5-(Trimethylsilyl)pent-2-en-4-ynoic acid 7 (Equation 4)

A 250 mL stainless steel autoclave was charged in the presence of air with PdI_2 (2.2 mg, 6.1 × 10^{-3} mmol), KI (10.1 mg, 6.1 × 10^{-2} mmol) and a solution or **7** (50.5 mg, 0.30 mmol) in a mixture of dioxane (8.2 mL) and MeOH (6.8 mL). The autoclave was sealed and, while the mixture was stirred, the autoclave was pressurized with CO (32 atm) and air (up to 40 atm). After being stirred at 80°C for 5 h, the autoclave was cooled, degassed and opened. The solvent was evaporated (first at 60 °C and 600 mmHg to remove MeOH, and then at 75 °C and 300 mmHg to remove dioxane), and the residue was subjected to column chromatography on silica gel using as eluent hexane to hexane/AcOEt 95:5. A mixture of methyl (*Z*)-2-[5-oxofuran-2(5*H*)-ylidene]acetate **8** and methyl (*E*)-2-[5-oxofuran-2(5*H*)-ylidene]-2-(trimethylsilyl)acetate **8'** (35 mg) was obtained, as confirmed by ^1H NMR analysis. From the proton spectrum, the **8**:**8'** ratio was about 1:0.8, which corresponded to a yield of **8** of about 41% and of **8'** of 24%. This mixture was further subjected to PTLC using hexane/AcOEt 93:7, which allowed to obtain ca. 15 mg of pure **8** (32% yield), while **8'** was still obtained impure with **8** (ca. 8 mg; **8'**:**8** ratio ca. 1:0.3, by ^{1}HNMR).

Mixture of methyl (*Z*)-2-[5-oxofuran-2(5*H*)-ylidene]acetate 8 and methyl (*E*)-2-[5-oxofuran-2(5*H*)-ylidene]-2-(trimethylsilyl)acetate 8'. Yield: 35 mg, starting from 50.5 mg of (*Z*)-5-(trimethylsilyl)pent-2-en-4-ynoic acid **7**. White solid. IR (KBr): ν = 1790 (s), 1713 (s), 1612 (m), 1558 (w), 1439 (m), 1235 (s), 1714 (m), 1042 (m), 826 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.39 (d, J = 5.3, 1 H, =CH, **8**), 7.83 (d, J = 5.3, 1 H, =CH, **8'**), 6.48 (d, J = 5.3, 1 H, =CH, **8**), 6.36 (d, J = 5.3, =CH, 1 H, **8'**), 5.95 (s, 1 H, =CHCO_2Me, 1 H, **8**), 3.81 (s, 3 H, CO_2Me for **8** + 3 H, CO_2Me for **8'**), 0.31 (s, 9 H, **8'**); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.83 (**8'**), 168.77 (**8'**), 167.8 (**8**), 165.3 (**8**), 161.4 (**8'**), 160.4 (**8**), 142.0 (**8**), 141.8 (**8'**), 124.5 (**8**), 122.6 (**8'**), 120.7 (**8'**), 102.2 (**8**), 52.1 (**8**+**8'**), –0.46 (**8'**); GC/MS: for **8**: m/z = 154 [M^+, 27], 123 (100), 95 (24), 69 (36); for **8'**: m/z = 226 [M^+, <0.5], 195 (3), 89 (100), 59 (22).

Methyl (*Z*)-2-[5-oxofuran-2(5*H*)-ylidene]acetate 8. Yield: 15.0 mg, starting from 50.5 mg of (*Z*)-5-(trimethylsilyl)pent-2-en-4-ynoic acid **7** (32%) White solid, mp = 59-60 °C. IR (KBr): ν = 1786 (s), 1709 (s), 1651 (m), 1443 (w), 1057 (w), 883 (w), 826 (s), 748 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.39 (d, J = 5.3, 1 H, =CH, **8**), 6.48 (d, J = 5.3, 1 H, =CH, **8**), 5.95 (s, 1 H, =CHCO_2Me, 1 H, **8**), 3.81 (s, 3 H, CO_2Me); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.8, 165.4, 160.4, 142.0, 124.5, 102.2, 52.1; GC/MS: m/z = 154 [M^+, 27], 123 (100), 95 (24), 69 (36).

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COMMUNICATION

A regio- and stereoselective carbonylative approach to alkyl (*Z*)-2-[3-oxoisobenzofuran-1-(3*H*)-ylidene]acetates

Adv. Synth. Catal. **Year**, *Volume*, Page – Page

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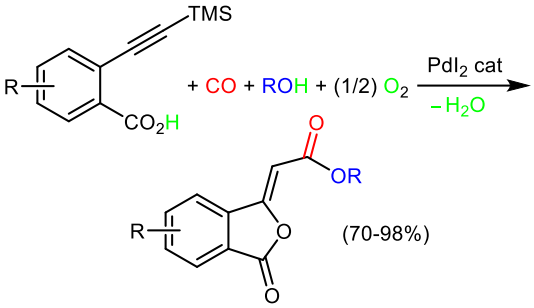

- *First example of oxidative carbonylation of 2-ethynylbenzoic acids leading to isobenzofuranones*
- *Completely regio- and stereoselective process*
- *TON up to 290 mol of product per mol of catalyst*