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Catalytic Carbonylative Double Cyclization of 2-(3-Hydroxy-1-yn-1-yl)phenols in Ionic Liquids Leading to Furobenzofuranone Derivatives

Raffaella Mancuso,*[,†] Rossana Miliè,[†] Antonio Palumbo Piccionello,[‡] Diego Olivieri,[§] Nicola Della Ca',[∥] Carla Carfagna,[§] and Bartolo Gabriele*[,†]

[†]Laboratory of Industrial and Synthetic Organic Chemistry (LISOC), Department of Chemistry and Chemical Technologies, University of Calabria, Via Pietro Bucci 12/C, 87036 Arcavacata di Rende, Cosenza, Italy

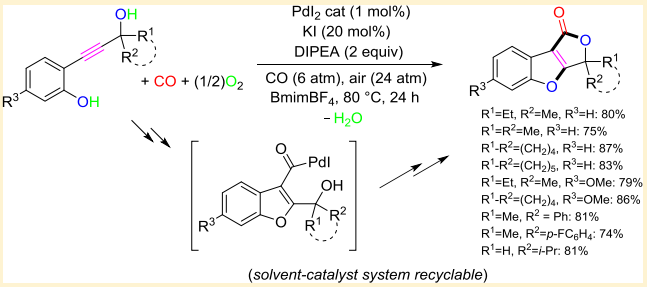
[‡]Department of Biological, Chemical and Pharmaceutical Science and Technology-STEBICEF, University of Palermo, Viale delle Scienze Ed. 17, 90128 Palermo, Italy

[§]Department of Industrial Chemistry "T. Montanari", University of Bologna, Viale Risorgimento 4, 40136 Bologna, Italy

[∥]Department of Chemistry, Life Sciences and Environmental Sustainability (SCVSA), University of Parma, Parco Area delle Scienze, 17/A, I-43124 Parma, Italy

Supporting Information

ABSTRACT: A catalytic carbonylative double cyclization method for the synthesis of furo[3,4-*b*]benzofuran-1(3*H*)-ones is reported. It is based on the reaction between readily available 2-(3-hydroxy-1-yn-1-yl)phenols, CO, and oxygen carried out in the presence of catalytic amounts of PdI_2 (1 mol %) in conjunction with KI (20 mol %) and 2 equiv of diisopropylethylamine at 80 °C for 24 h under 30 atm of a 1:4 mixture of CO−air. Interestingly, the process was not selective when carried out in classical organic non-nucleophilic solvents (such as MeCN or DME), leading to a mixture of the benzofurofuranone derivative and the benzofuran ensuing from simple cycloisomerization, whereas it turned out chemoselective toward the formation of the double cyclization compound in $BmimBF_4$ as the reaction medium. Moreover, the ionic liquid solvent containing the catalyst could be easily recycled several times without appreciable loss of activity.



INTRODUCTION

Palladium-catalyzed double cyclization processes are a powerful method for the construction of complex functionalized molecules starting from readily available acyclic substrates in a single operation, and impressive progress has been made in this field during the last decades.[1,2] In particular, we have very recently developed in our laboratories important processes of this kind, under oxidative carbonylative conditions and with the promotion of a very simple catalytic system, consisting of PdI_2 in conjunction with an excess of KI,[3] with molecular oxygen as oxidant. Thus, dihydrofurofuranones with antitumor activity[4] and furo[3,4-*b*]indol-1-ones[5] were obtained in good to high yields from CO, O_2, and 4-yne-1,3-diols or 3-(2-aminophenyl)prop-2-yn-1-ols, respectively.

In this work, we report a remarkable example of the synthesis of furo[3,4-*b*]benzofuran-1(3*H*)-ones by oxidative carbonylative double cyclization of 2-(3-hydroxy-1-yn-1-yl)-phenols carried out under catalytic conditions (1 mol % of PdI_2 in conjunction with 20 mol % of KI) and with the possibility to easily recycle the catalyst. To the best of our knowledge, this scaffold has so far been constructed by only two other methods, which are the reaction between 2-iodophenols and tetronic acid in a basic ionic liquid (IL)[6] and the $PdCl_2(PPh_3)_2$-promoted carbonylative double cyclization of 2-(3-hydroxy-1-yn-1-yl)phenols, conducted under stoichiometric conditions.[7]

RESULTS AND DISCUSSION

PdI_2/KI-Catalyzed Carbonylative Double Cyclization of 2-(3-Hydroxy-1-yn-1-yl)phenols 1 to Furo[3,4-*b*]-benzofuran-1(3*H*)-ones 2 in Conventional Solvents. We first tested 2-(3-hydroxy-3-methylpent-1-yn-1-yl)phenol **1a** (readily prepared by Sonogashira coupling between 2-iodophenol and 3-methylpent-1-yn-3-ol, see the Experimental Section for details), which was allowed to react with CO and O_2 under conditions similar to those used before for the synthesis of furo[3,4-*b*]indol-1-ones.[5] Using 2 mol % of PdI_2 and 20 mol % of KI,[8] under 6 atm of CO and 24 atm of air, in MeCN as the solvent (0.25 mmol of **1a** per mL of MeCN) at

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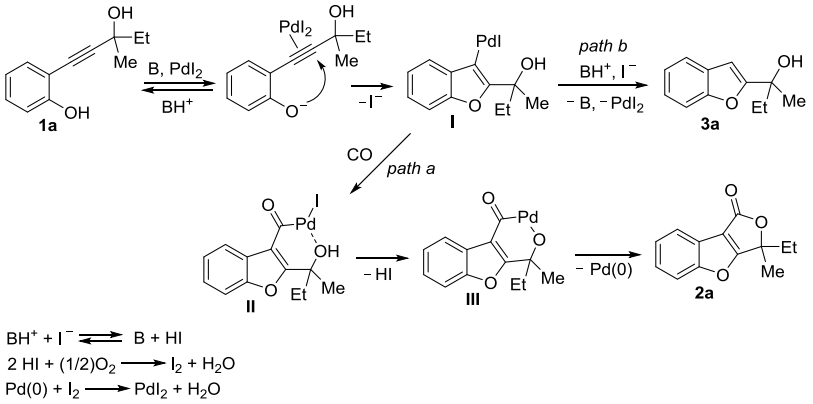
Scheme 1. Mechanistic Hypotheses for the PdI_2-Catalyzed Carbonylative Double Cyclization of 2-(3-Hydroxy-3-methylpent-1-yn-1-yl)phenol 1a under Oxidative Conditions Leading to 3-Ethyl-3-methylfuro[3,4-*b*]benzofuran-1(3*H*)-one 2a (Path a) and the PdI_2-Catalyzed Cycloisomerization of 1a To Give 2-(Benzofuran-2-yl)butan-2-ol 3a (Path b) (B = Base)

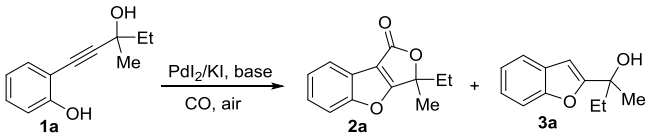


80 °C for 15 h, no reaction took place. Considering the low nucleophilicity of the phenolic hydroxyl, we then tried the same reaction in the presence of a base (B) to favor the formation in situ of the more nucleophilic phenate oxygen, more prone to attack the triple bond coordinated to the metal center (Scheme 1; anionic iodide ligands are omitted for clarity). The vinylpalladium species **I** resulting from 5-endo-dig cyclization would then undergo carbon monoxide insertion to give complex **II**, from which the final carbonylated double cyclization product **2a** would be formed by intramolecular trapping by the alcoholic hydroxyl (possibly through the formation of a palladacycle intermediate **III**); the ensuing Pd(0) would then be reoxidized by oxygen (Scheme 1, pathway a).

According to this hypothesis, using the same conditions as above, but in the presence of morpholine as the base, the desired product (3-ethyl-3-methylfuro[3,4-*b*]benzofuran-1(3*H*)-one, **2a**) was indeed formed, albeit in low yield (14%; Table 1, entry 2). Analysis of the reaction mixture also evidenced the formation of smaller amounts (11% yield) of 2-(benzofuran-2-yl)butan-2-ol **3a** (from a simple cycloisomerization process, ensuing from protonolysis of intermediate **I**, Scheme 1, pathway b) together with chromatographically immobile materials, deriving from substrate decomposition, which were not investigated further. Gratifyingly, using diisopropylethylamine (DIPEA) instead of morpholine led to a significant higher yield of **2a** up to 55%, **3a** being still formed in 20% yield (Table 1, entry 3). To further improve these initial promising results, we changed the reaction operative parameters, such as temperature, pressure, and so on; the results obtained are shown in Table 1, entries 4–12. As can be seen from the table, better results in terms of yield and selectivity toward the carbonylated product **2a** were obtained by carrying out the process in MeCN under more diluted conditions, still at 80 °C and under 30 atm of a 1:4 mixture of CO–air (yields of **2a** and **3a** were 65 and 5%, respectively, Table 1, entry 10). The reaction could successfully be performed even with a lower catalyst loading (1 mol % of PdI_2), again with good results (Table 2, entry 1).

We then assessed the generality of the process starting from differently substituted substrates; the results are shown in Table 2, entries 2–7. As could be expected, 2-(3-hydroxy-3-methylbut-1-yn-1-yl)phenol **1b** behaved similarly to **1a** (Table 2, entry 2). 2-[(1-Hydroxycyclopentyl)ethynyl]phenol **1c** led to the corresponding tetracyclic product in 74% yield (Table 2,

Table 1. PdI_2/KI-Catalyzed Reactions of 2-(3-Hydroxy-3-methylpent-1-yn-1-yl)phenol 1a under Oxidative Carbonylation Conditions in Conventional Solvents[a,b]



entry	solvent	base	concn. of **1a**[c]	*T* (°C)	yield of **2a**[d] (%)	yield of **3a**[d] (%)
1[e]	MeCN	none	0.25	80		
2	MeCN	morpholine	0.25	80	14	11
3	MeCN	DIPEA	0.25	80	55	20
4	MeCN	DIPEA	0.25	100	35	12
5	MeCN	DIPEA	0.25	70	53	17
6	MeCN	DIPEA	0.25	60	45	12
7	DME	DIPEA	0.25	80	34	10
8[e]	dioxane	DIPEA	0.25	80		
9	MeCN	DIPEA	0.10	80	50	22
10	MeCN	DIPEA	0.05	80	65	5
11[f]	MeCN	DIPEA	0.05	80	28	5
12[g]	MeCN	DIPEA	0.05	80	21	2

[a]Unless otherwise noted, all reactions were carried out for 15 h in the presence of 2 mol % of PdI_2, 20 mol % of KI, and 2 equiv of base, under 30 atm of a 1:4 mixture of CO–air. [b]Unless otherwise noted, substrate conversion was quantitative. [c]mmol of **1a** per mL of solvent. [d]Based on starting **1a**. [e]No reaction took place. [f]The reaction was carried out under 60 atm of a 1:4 mixture of CO–air. [g]The reaction was carried out under 20 atm of a 4:1 mixture of CO–air.

entry 3). The substrate conversion rate was slightly slower in the presence of a methoxy group at C-5, as in **1d**, or when the alkyl group α to the alcoholic hydroxyl was replaced by a phenyl, as in **1e**. In fact, these substrates achieved complete conversion after 15 h instead of 8 h, with a yield of the corresponding furobenzofuranones **2d** and **2e** of 60 and 57%, respectively (Table 2, entries 4 and 5, respectively). However, no cyclocarbonylation took place with a substrate bearing a secondary alcoholic function, such as **1f**, which afforded the benzofuran product **3f** deriving from simple cycloisomerization. These results suggest that the second cyclization step (cyclocarbonylation by intramolecular trapping of acylpalladium complex **II** by the alcoholic hydroxyl; Scheme 1, path a) is strongly favored, with respect to protonolysis, leading to cycloisomerization product **3** (Scheme 1, path b), by the

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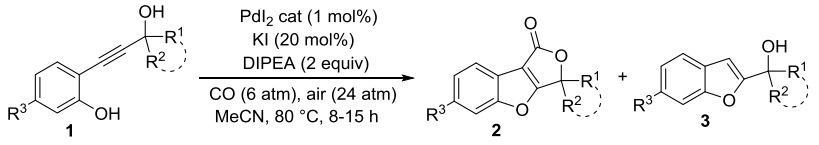
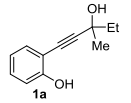
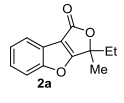
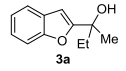
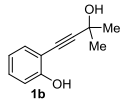
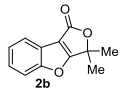
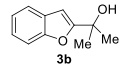
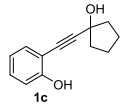
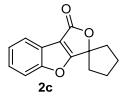
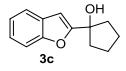
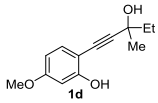
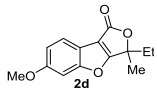
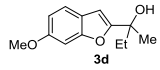
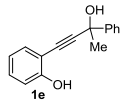
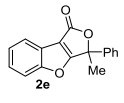
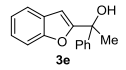
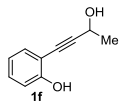
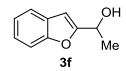
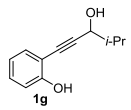
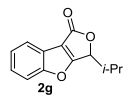
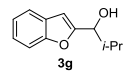
Table 2. PdI_2/KI-Catalyzed Oxidative Carbonylation of 2-(3-Hydroxy-1-yn-1-yl)phenols 1 in MeCN[a]



Entry	1	t (h)	2	Yield of 2[b] (%)	3	Yield of 3[b] (%)
1	 1a	8	 2a	68	 3a	5
2	 1b	8	 2b	60	 3b	9
3	 1c	8	 2c	74	 3c	22
4	 1d	15	 2d	60	 3d	10
5	 1e	15	 2e	57	 3e	20
6	 1f	8			 3f	58
7	 1g	8	 2g	63	 3g	5

[a]All reactions were carried out at 80 °C under 30 atm (at 25 °C) of a 1:4 mixture of CO−air, in MeCN as the solvent (substrate concentration: 0.05 mmol of **1** per mL of solvent), and in the presence of 1 mol % of PdI_2, 20 mol % of KI, and 2 equiv of DIPEA. [b]Based on starting **1**.

reactive rotamer effect[9] exerted by the geminal substituents at the alcoholic carbon. To verify this hypothesis, we also synthesized and tested the reactivity of 2-(3-hydroxy-4-methylpent-1-yn-1-yl)phenol **1g**, bearing a single but bulky substituent (isopropyl) α to the alcoholic group, able to exert a sufficient steric effect to allow for an efficient second cyclization. In perfect agreement with this hypothesis, substrate **1g** was converted into the corresponding carbonylated product in good yield (63%, Table 2, entry 7), comparable to that obtained with α,α-dialkylsubstituted 2-(3-hydroxy-1-yn-1-yl)-phenols **1a**−**e**.[10]

PdI_2/KI-Catalyzed Carbonylative Double Cyclization of 2-(3-Hydroxy-1-yn-1-yl)phenols 1 to Furo[3,4-*b*]-benzofuran-1(3*H*)-ones 2 in ILs. Considering that, under certain circumstances, the use of unconventional solvents such as ILs may affect the selectivity of catalytic processes and may also permit the recycle of the catalytic system,[11] we also performed our reaction in different ILs as the reaction medium. The results obtained with **1a**, reported in Table 3, allowed us to draw the following conclusions: (a) the process took place in all the ILs tested, even though with different performances in terms of substrate conversion rate and product yield; (b) the optimal reaction time was 24 h, substrate conversion being incomplete after 15 h (Table 3, entry 1); (c) with the exception of $Mor_{1,2}N(CN)_2$ (Table 3, entry 7), the desired cyclocarbonylated product **2a** was formed selectively in a consistent manner (Table 3, entries 1−5); (d) as in the case of the reaction carried out in MeCN (Table 1, entry 1), no reaction took place in the absence of the base (Table 3, entry 6); (e) the best results in terms of **2a** yield

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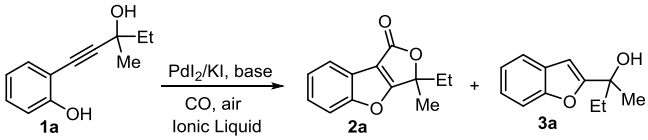
Table 3. PdI_2/KI-Catalyzed Reactions of 2-(3-Hydroxy-3-methylpent-1-yn-1-yl)phenol 1a under Oxidative Carbonylation Conditions in Different ILs.[a,b]



entry	IL	t (h)	substrate conversion[b]	yield of **2a**[c] (%)	yield of **3a**[c] (%)
1	$BmimBF_4$	15	65	59	
2	$BmimBF_4$	24	100	80	
3	BmimCl	24	68	20	
4	$BmimPF_6$	24	100	51	
5	$EmimEtSO_4$	24	100	67	
6[d]	$EmimEtSO_4$	24	NR		
7	$Mor_{1,2}N(CN)_2$	24	100	53	10
8[e]	$BmimBF_4$	24	100	75	

[a]Unless otherwise noted, all reactions were carried out at 80 °C under 30 atm (at 25 °C) of a 1:4 mixture of CO−air, in an IL as the solvent (substrate concentration: 0.05 mmol of **1a** per mL of solvent, 0.5 mmol scale), and in the presence of 1 mol % of PdI_2, 20 mol % of KI, and 2 equiv of DIPEA. [b]Determined by GLC. [c]Based on starting **1a**. [d]The experiment was carried out in the absence of DIPEA. NR = no reaction. [e]The experiment was carried out on a larger scale (2.5 mmol of **1a**).

(80%) were observed with 1-butyl-3-methylimidazolium tetrafluoroborate ($BmimBF_4$; Table 3, entry 2).[12] An experiment carried out in this IL on a larger scale (2.5 mmol of **1a** rather than 0.5 mmol) also led to satisfactory results (the yield of **2a** was 75%, Table 3, entry 8).

Our next step was to assess the possibility to recycle the catalyst and to generalize the process to other variously substituted substrates, using $BmimBF_4$ as unconventional solvent. The results obtained with 2-(3-hydroxy-1-yn-1-yl)-phenols **1a−g**, already tested in MeCN, together with the additional substrates **1h−j** (bearing different α,α-dialkyl substituents) are shown in Table 4. Gratifyingly, the process turned out to be selective toward the formation of the corresponding furobenzofuranones **2** with all the α,α-dialkylsubstituted substrates examined **1a−e** and **1h−j** (Table 4, entries 1−5 and 7−9, respectively) as well as with substrate **1g** bearing a bulky isopropyl group α to the alcoholic function (Table 4, entry 6), with yields ranging from 74 to 87%.[13] Moreover, the catalytic system dissolved in the IL medium could be easily recycled up to six times without appreciable loss of activity. In detail, after extraction of the product with diethyl ether, fresh substrate and DIPEA were added to the residue, and the carbonylation was carried out again under the same conditions of the parent experiment.

CONCLUSIONS

We have reported the first example of carbonylative double cyclization of 2-(3-hydroxy-1-yn-1-yl)phenols (α,α-dialkylsubstituted or α-monosubstituted with a sufficiently bulky group) carried out under catalytic conditions. The process, leading to tricyclic furo[3,4-*b*]benzofuran-1(3*H*)-ones in one synthetic step from readily available substrates, is catalyzed by a simple system, consisting of PdI_2 (1 mol %) in conjunction with KI (20 mol %) and takes place in the presence of DIPEA as the base (2 equiv) and molecular oxygen as the oxidant. Either a classical non-nucleophilic organic solvent (such as MeCN) or an unconventional solvent such as $BmimBF_4$ can be used as reaction medium; however, better selectivities and yields are observed in the latter case, with the additional advantage of catalyst recyclability.

EXPERIMENTAL SECTION

General Experimental Methods. Solvents and chemicals were of reagent grade and were used without further purification. All reactions were analyzed by thin-layer chromatography on silica gel 60 F254 and by gas−liquid chromatography (GLC) using capillary columns with polymethylsilicone + 5% phenylsilicone as the stationary phase. Column chromatography was performed on silica gel 60 (70−230 mesh) or neutral alumina (90−170). Evaporation refers to the removal of solvent under reduced pressure. Melting points are uncorrected. ^1H NMR and $^{13}C\{^1H\}$ NMR spectra were recorded at 25 °C on a 300 spectrometer in $CDCl_3$ and DMSO-d_6 with Me_4Si as internal standard. $^{19}F\{^1H\}$ NMR spectra were recorded on a 500 spectrometer in $CDCl_3$ solutions at 471 MHz with $CFCl_3$ as internal standard. Chemical shifts (δ) and coupling constants (J) are given in ppm and in Hz, respectively. Infrared (IR) spectra were taken with a Fourier transform-IR spectrometer. Mass spectra were obtained using a gas chromatography (GC)/mass spectrometry (MS) apparatus at 70 eV ionization voltage (normal resolution) and by electrospray ionization MS (ESI-MS) (high-resolution) with an ultra-high-definition accurate-mass quadrupole time of flight spectrometer equipped with a Dual AJS ESI source working in positive mode, and were recorded in the 150−1000 m/z range. The LC−MS experimental conditions were as follows: 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 350 °C and a flow of 12 L/min. A potential of 3.5 kV was used on the capillary for positive ion mode. The fragmentor was set to 175 V.

Preparation of Substrates 1a−j. 2-(3-Hydroxy-1-yn-1-yl)-phenols **1** was prepared by Sonogashira coupling between commercially available 2-iodophenols and propargyl alcohols according to the following procedure. A solution of 2-iodophenol (1.0 g, 4.55 mmol) or 5-methoxy-2-iodophenol (1.14 g, 4.55 mmol), $PdCl_2(PPh_3)_2$ (32.0 mg, 0.045 mmol), CuI (7.0 mg, 0.036 mmol), and propargyl alcohol [5.63 mmol; 3-methylpent-1-yn-3-ol, 552.6 mg; 2-methylbut-3-yn-2-ol, 473.6 mg; 1-ethynylcyclopenten-1-ol, 620.2 mg; 2-phenylbut-3-yn-2-ol, 823.6 mg; but-3-yn-2-ol, 394.5 mg; 1-phenylprop-2-yn-1-ol, 744.1 mg; 4-methylpent-1-yn-3-ol, 552.6 mg; 1-ethynylcyclohexan-1-ol, 699.1 mg; 2-(4-fluorophenyl)but-3-yn-2-ol, 924.3 mg] in Et_3N (12 mL) was allowed to stir for 4 h (for **1a**, **1c**, **1e**, **1h**, and **1j**), 5 h (for **1d** and **1i**), or 6 h (**1b**, **1f**, and **1g**) at room temperature under nitrogen. Saturated solutions of NH_4Cl (50 mL) and CH_2Cl_2 (30 mL) were sequentially added. The phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL). The aqueous phase was acidified either with 1 M HCl until pH = 5 (for **1a−d**, **1f**, **1g−i**) or with 0.1 M HCl (3 × 50 mL) (for **1e** and **1j**). Et_2O (100 mL) was added to the resulting aqueous phase, the phases were separated, and the aqueous phase was extracted with Et_2O (3 × 100 mL). All the collected organic layers were washed with H_2O (until neutral pH) and brine (40 mL) and then dried over Na_2SO_4. After filtration and evaporation of the solvent, the product was purified by column chromatography on silica gel using as eluent hexane−AcOEt from 99:1 to 9:1 (for **1a−h**), $CHCl_3$/MeOH from 99:1 to 98:2 (for **1i**), or $CHCl_3$/MeOH from 99:1 to 95:5 (for **1j**).

2-(3-Hydroxy-3-methylpent-1-yn-1-yl)phenol (1a). Yield: 691.2 mg, starting from 1.0 g of 2-iodophenol (80%). White solid, mp = 43−45 °C. IR (KBr) ν: 3383 (m, br), 3089 (s, br), 2231 (w), 1449 (m), 1125 (m), 754 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.29 (d, J = 7.6, 1H), 7.22 (t, J = 7.7, 1H), 6.95 (d, J = 8.2, 1H), 6.83 (t, J = 7.4, 1H), 6.77 (s, br, 1H), 3.20 (s, br, 1H), 1.92−1.73 (m, 2H), 1.60 (s, 3H), 1.10 (t, J = 7.4, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 156.9, 131.8, 130.3, 120.1, 115.2, 109.1, 99.0, 78.3, 69.7, 36.6, 29.2, 9.2. GC/MS m/z: 190 (M^+, 5), 172 (69), 161 (30), 157 (45). HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{12}H_{14}O_2Na^+$, 213.0886; found, 213.0886.

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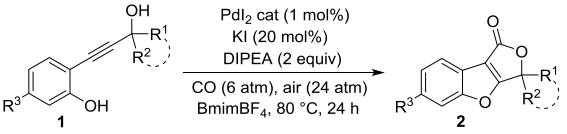
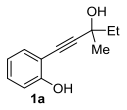
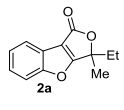
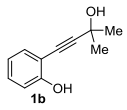
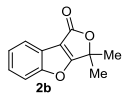
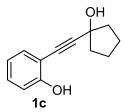
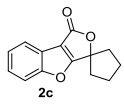
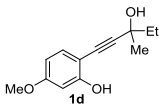
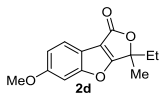
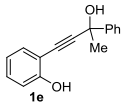
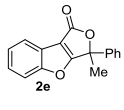
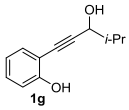
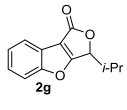
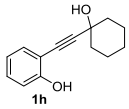
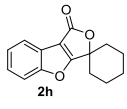
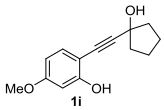
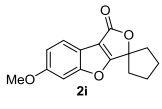
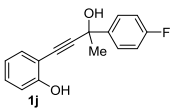
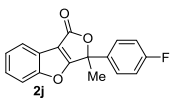
Table 4. Synthesis of Furo[3,4-*b*]benzofuran-1(3*H*)-ones 2 by PdI_2/KI-Catalyzed Oxidative Carbonylation of 2-(3-Hydroxy-1-yn-1-yl)phenols 1 in $BmimBF_4$[a]



Entry	1	2	Yield of 2[b] (%)						
			Run 1	Run 2	Run 3	Run 4	Run 5	Run 6	Run 7
1	 1a	 2a	80	80	79	79	79	78	78
2	 1b	 2b	75	77	77	76	76	75	74
3	 1c	 2c	87	86	84	85	86	84	84
4	 1d	 2d	79	78	78	77	77	77	78
5	 1e	 2e	81	80	80	80	79	78	79
6	 1g	 2g	81	82	80	80	79	79	78
7	 1h	 2h	83	82	82	82	81	81	81
8	 1i	 2i	86	86	87	85	86	87	86
9	 1j	 2j	74	74	73	73	72	74	72

[a]All reactions were carried out at 80 °C under 30 atm (at 25 °C) of a 1:4 mixture of CO−air, in $BmimBF_4$ as the solvent (substrate concentration: 0.05 mmol of **1** per mL of solvent), and in the presence of 1 mol % of PdI_2, 20 mol % of KI, and 2 equiv of DIPEA. [b]Based on starting **1**. The first run corresponds to the parent experiment, the next runs to recycles. See the text for details.

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*2-(3-Hydroxy-3-methylbut-1-yn-1-yl)phenol (**1b**).* Yield: 576.3 mg, starting from 1.0 g of 2-iodophenol (72%). White solid, mp = 131−132 °C lit.,[14] 131−132 °C. IR (KBr) ν: 3393 (s), 3084 (s, br), 2224 (w), 1450 (m), 1285 (m), 1154 (s), 761 (m) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 9.65 (s, 1H), 7.27 (dd, J = 7.6, 1.6, 1H), 7.23−7.13 (m, 1H), 6.94 (dist d, J = 8.2, 1H), 6.83−6.74 (m, 1H), 5.48 (s, br, 1H), 1.53 (s, 6H). $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 158.4, 133.2, 129.8, 119.4, 115.8, 110.4, 99.5, 77.9, 64.3, 32.1. GC/MS m/z: 176 (M^+, 9), 158 (100), 143 (31), 131 (14), 115 (18). The spectroscopic data agreed with those reported.[14]

*2-[(1-Hydroxycyclopentyl)ethynyl]phenol (**1c**).* Yield: 688.8 mg, starting from 1.0 g of 2-iodophenol (75%). Yellow solid, mp = 95−96 °C. IR (KBr) ν: 3378 (s, br), 3078 (s, br), 2224 (w), 1454 (m), 989 (s), 752 (m) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 9.72 (s, 1H), 7.22 (dd, J = 7.6, 1.6, 1H), 7.19−7.11 (m, 1H), 6.87 (dist d, J = 8.2, 1H), 6.76 (td, J = 7.5, 1.0, 1H), 5.26 (s, 1H), 1.90−1.81 (m, 4H), 1.80−1.61 (m, 4H). $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 158.4, 133.2, 129.8, 119.3, 115.8, 110.6, 98.5, 78.8, 73.4, 42.5, 23.5. GC/MS m/z: 202 (M^+, 5), 201 (6), 184 (100), 169 (42), 145 (28), 131 (32). HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{13}H_{14}O_2Na^+$, 225.0886; found, 225.0890.

*2-(3-Hydroxy-3-methylpent-1-yn-1-yl)-5-metoxyphenol (**1d**).* Yield: 500.3 mg, starting from 1.14 g of 5-metoxy-2-iodophenol (50%). Yellow solid, mp = 105−107 °C. IR (KBr) ν: 3373 (s, br), 3130 (s, br), 2223 (w), 1321 (m), 1260 (s), 1031 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.19 (d, J = 8.5, 1H), 6.51 (d, J = 2.3, 1H), 6.42 (dd, J = 8.5, 2.3, 1H), 3.78 (s, 3H), 2.75 (s, br, 1H), 1.90−1.72 (m, 2H), 1.60 (s, 3H), 1.10 (t, J = 7.4, 3H) (*Note*: one −OH signal was too broad to be detected). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 161.5, 158.2, 132.5, 107.1, 101.4, 100.3, 98.1, 78.0, 69.6, 55.4, 36.6, 29.4, 9.2. GC/MS m/z: 220 (M^+, 31), 202 (100), 191 (60), 187 (80), 149 (18). HRMS (ESI-TOF) m/z: $[M-H_2O + H]^+$ calcd for $C_{13}H_{15}O_2^+$, 203.1067; found, 203.1066.

*2-[(3-Hydroxy-3-cyclopentyl)ethynyl]phenol (**1e**).* Yield: 736.1 mg, starting from 1.0 g of 2-iodophenol (68%). White solid, mp = 78−79 °C. IR (KBr) ν: 3333 (s, br), 2237 (vw), 1453 (m), 1056 (w), 764 (s), 699 (s) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.66 (d, J = 7.5, 2H), 7.43−7.17 (m, 5H), 6.93 (d, J = 8.2, 1H), 6.84 (t, J = 7.5, 1H), 6.60 (s, 1H), 3.48 (s, br, 1H), 1.86 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 157.0, 145.0, 132.0, 130.6, 128.5, 128.0, 124.9, 120.3, 115.3, 108.9, 99.0, 79.7, 70.7, 33.1. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{16}H_{14}O_2Na^+$, 261.0886; found, 261.0879. The spectroscopic data agreed with those reported.[15]

*2-(3-Hydroxybut-1-yn-1-yl)phenol (**1f**).* Yield: 515.3 mg, starting from 1.0 g of 2-iodophenol (70%). White solid, mp = 73−74 °C. IR (KBr) ν: 3372 (s, br), 2226 (w), 1485 (m), 1451 (s), 1289 (m), 1030 (m), 752 (s) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.27 (dd, J = 7.7, 1.5, 1H), 7.25−7.17 (m, 1H), 6.98−6.91 (m, 1H), 6.82 (td, J = 7.5, 1.1, 1H), 4.82 (q, J = 6.6, 1H), 2.17 (s, 1H), 1.56 (d, J = 6.6) (*Note*: the phenolic −OH signal was too broad to be detected). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 156.9, 131.9, 130.5, 120.2, 115.3, 109.0, 97.1, 79.0, 59.0, 24.3. GC/MS m/z: 162 (M^+, 25), 144 (100), 115 (56), 91 (60). HRMS (ESI-TOF) m/z: $[M-H_2O + H]^+$ calcd for $C_{10}H_9O^+$, 145.0648; found, 145.0650.

*2-(3-Hydroxy-4-methylpent-1-yn-1-yl)phenol (**1g**).* Yield: 535.6 mg, starting from 1.0 g of 2-iodophenol (62%). Yellow solid, mp = 81−82 °C. IR (KBr) ν: 3381 (m, br), 3077 (m, br), 2223 (w), 1451 (s), 1385 (m), 1011 (s), 748 (s) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.30 (dd, J = 7.8, 1.8, 1H), 7.27−7.18 (m, 2H), 6.96 (dd, J = 8.3, 1.0, 1H), 6.84 (td, J = 7.5, 1.0, 1H), 4.47 (d, J = 5.6, 1H), 2.08−1.92 (m, 1H), 1.08 (d, J = 6.8, 3H), 1.05 (d, J = 6.8, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 157.0, 131.9, 130.4, 120.2, 115.2, 109.1, 95.1, 80.5, 68.6, 34.6, 18.2, 17.6. GC/MS m/z: 190 (M^+, 9), 172 (20), 147 (45), 91 (100). The spectroscopic data agreed with those reported.[7]

*2-[(1-Hydroxycyclohexyl)ethynyl]phenol (**1h**).* Yield: 589.3 mg, starting from 1.0 g of 2-iodophenol (60%). Yellow solid, mp = 114−116 °C. IR (KBr) ν: 3485 (m, br), 3330 (m, br), 3149 (m, br), 2219 (w), 1489 (m), 1453 (s), 1055 (m), 752 (s) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.29 (dd, J = 7.7, 1.6, 1H), 7.24−7.17 (m, 1H), 6.95 (dd, J = 8.3, 0.6, 1H), 6.89−6.79 (m, 2H), 3.49 (s, br, 1H), 2.12−1.97 (m, 2H), 1.79−1.48 (m, 7H), 1.35−1.17 (m, 1H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 156.9, 131.9, 130.3, 120.1, 115.3, 109.2, 99.1, 79.3, 69.7, 40.0, 25.1, 23.4. GC/MS m/z: 216 (M^+, 5), 198 (100), 183 (41), 170 (71), 131 (26). The spectroscopic data agreed with those reported.[7]

*2-[(1-Hydroxycyclopentyl)ethynyl]-5-methoxyphenol (**1i**).* Yield: 528.4 mg, starting from 1.14 g of 5-methoxy-2-iodophenol (50%). White solid, mp = 137−138 °C. IR (KBr) ν: 3330 (s, br), 3083 (m, br), 2220 (m), 1518 (m), 1425 (m), 1209 (s), 1032 (m), 993 (m) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 9.77 (s, 1H), 7.13 (d, J = 8.5, 1H), 6.41 (d, J = 1.8, 1H), 6.36 (dd, J = 8.5, 1.8, 1H), 5.19 (s, 1H), 3.70 (s, 3H), 1.94−1.79 (m, 4H), 1.79−1.59 (m, 4H). $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 160.1, 159.1, 133.5, 105.1, 102.6, 100.9, 96.5, 78.3, 72.6, 54.2, 42.0, 23.0. GC/MS m/z: 232 (M^+, 17), 214 (100), 199 (36), 189 (12), 161 (11), 115 (13). HRMS (ESI-TOF) m/z: $[M-H_2O + H]^+$ calcd for $C_{14}H_{15}O_2^+$, 215.1067; found, 215.1062.

*2-[3-(4-Fluorophenyl)-3-hydroxybut-1-yn-1-yl]phenol (**1j**).* Yield: 814.5 mg, starting from 1.0 g of 2-iodophenol (70%). White solid, mp = 95−96 °C. IR (KBr) ν: 3336 (s, br), 3067 (m, br), 2240 (w), 1589 (m), 1455 (s), 1270 (m), 1089 (m), 751 (s) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 10.0 (s, br, 1H), 7.60−7.35 (m, 3H), 7.30 (d, J = 7.6, 1H), 7.25−7.04 (m, 2H), 6.91 (d, J = 8.1, 1H), 6.80 (t, J = 7.4 1H), 6.30 (s, br, 1H), 1.71 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 162.2 (d, J = 242.7), 158.3, 150.3 (d, J = 6.9), 132.7, 129.8, 121.4 (d, J = 2.8), 118.9, 115.3, 113.7 (d, J = 20.8), 112.0 (d, J = 22.9), 109.5, 96.7, 80.4, 68.2, 33.7. $^{19}F\{^1H\}$ NMR (471 MHz, $CDCl_3$): δ −112.7. HRMS (ESI-TOF) m/z: $[M-H_2O + H]^+$ calcd for $C_{16}H_{12}FO^+$, 239.0867; found, 239.0857.

Preparation of ILs. ILs 1-butyl-3-methylimidazolium chloride (BmimCl),[16] 1-butyl-3-methylimidazolium hexafluorophosphate ($BmimPF_6$),[16] 1-butyl-3-methylimidazolium tetrafluoroborate ($BmimBF_4$),[16] 1-ethyl-3-methylimidazolium ethyl sulfate (EmimEt-SO_4),[17] and *N*-ethyl-*N*-methylmorpholinium dicyanamide [$Mor_{1,2}N$-$(CN)_2$][17] were prepared according to literature procedures: the structure and purity of all ILs were confirmed by ^1H and ^{13}C NMR spectroscopy.

General Procedure for the Cyclization of 2-(3-Hydroxy-1-yn-1-yl)phenols 1a−h in MeCN under Oxidative Carbonylation Conditions (Table 2). A 250 mL stainless-steel autoclave was charged in the presence of air with PdI_2 (1.9 mg, 5.3×10^{-3} mmol), KI (17.5 mg, 0.105 mmol), DIPEA (136 mg, 1.05 mmol), and compounds **1** (0.53 mmol; 101.0 mg, **1a**; 93.2 mg, **1b**; 107.5, **1c**; 117.2 mg, **1d**; 126.6 mg, **1e**; 86.2 mg, **1f**; 101.0 mg, **1g**) in 10.5 mL of MeCN. The autoclave was pressurized with CO (6 atm) and air (up to 30 atm). After stirring at 80 °C for 8−15 h (see Table 2), the autoclave was cooled and degassed. The solvent was evaporated, and the crude products purified by column chromatography on silica gel (eluent: 99:1 to 9:1 hexane−ethyl acetate) to give pure furobenzofurane derivatives **2** (78.2 mg, 68%, **2a**; 64.6 mg, 60%, **2b**; 89.7 mg, 74%, **2c**; 78.6 mg, 60%, **2d**; 80.0 mg, 57%, **2e**; 72.5 mg, 63%, **2g**) and benzofuran derivatives **3** (5.2 mg, 5%, **3a**; 8.6 mg, 9%, **3b**; 23.7 mg, 22%, **3c**; 11.4 mg, 10%, **3d**; 25.7 mg, 20%, **3e**; 50.1 mg, 58%, **3f**; 5.2 mg, 5%, **3g**). The isolated yields obtained in each experiment are given in Table 2.

*3-Ethyl-3-methylfuro[3,4-b]benzofuran-1(3H)-one (**2a**).* Yield: 78.2 mg, starting from 101.0 mg of 2-(3-hydroxy-3-methylpent-1-yn-1-yl)phenol (68%). Yellow solid, mp = 40−41.0 °C. IR (KBr) ν: 1773 (s), 1616 (m), 1443 (m), 1155 (m), 1083 (m), 942 (m), 877 (m), 752 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.86−7.77 (m, 1H), 7.63−7.54 (m, 1H), 7.46−7.35 (m, 2H), 2.08 (q, J = 7.4, 2H), 1.74 (s, 3H), 0.93 (t, J = 7.4, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 182.1, 163.7, 161.6, 125.7, 125.0, 121.21, 121.15, 112.7, 112.2, 84.2, 31.1, 23.4, 8.1. GC/MS m/z: 216 (M^+, 28), 201 (7), 187 (100), 173 (49), 145 (47). HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{13}H_{13}O_3^+$, 217.0859; found, 217.0861.

*3,3-Dimethylfuro[3,4-b]benzofuran-1(3H)-one (**2b**).* Yield: 64.6 mg, starting from 93.2 mg of 2-(3-hydroxy-3-methylbut-1-yn-1-yl)phenol (60%). Colorless solid, mp = 59−60 °C. IR (KBr) ν: 1760 (s), 1626 (m), 1161 (m), 1080 (m), 761 (m) cm^{-1}; ^1H NMR

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(300 MHz, $CDCl_3$): δ 7.84−7.76 (m, 1H), 7.61−7.54 (m, 1H), 7.44−7.36 (m, 2H), 1.77 (s, 6H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 182.9, 163.4, 161.5, 125.8, 125.1, 121.3, 121.2, 112.7, 111.2, 81.1, 25.1. GC/MS *m/z*: 202 (M^+, 44), 187 (69), 159 (100), 145 (49). HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{12}H_{11}O_3^+$, 203.0703; found, 203.0706.

1′H-Spiro[cyclopentane-1,3′-furo[3,4-b]benzofuran]-1′-one (**2c**). Yield: 89.7 mg, starting from 107.5 mg of 2-[(1-hydroxycyclopentyl)-ethynyl]phenol (74%). Yellow solid, mp = 53−55 °C. IR (KBr) ν: 1768 (s), 1443 (m), 1085 (m), 952 (m), 756 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.85−7.74 (m, 1H), 7.63−7.51 (m, 1H), 7.45−7.33 (m, 2H), 2.37−1.87 (m, 8H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 180.8, 163.7, 161.7, 125.7, 125.0, 121.4, 121.1, 112.7, 112.0, 90.5, 36.9, 24.8. GC/MS *m/z*: 228 (M^+, 100), 200 (89), 171 (79), 159 (48), 144 (83), 115 (25). HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{14}H_{13}O_3^+$, 229.0859; found, 229.0866.

3-Ethyl-6-methoxy-3-methylfuro[3,4-b]benzofuran-1(3H)-one (**2d**). Yield: 78.6 mg, starting from 117.2 mg of 2-(3-hydroxy-3-methylpent-1-yn-1-yl)-5-metoxyphenol (60%). Yellow solid, mp = 73−75 °C. IR (KBr) ν: 1777 (s), 1499 (w), 1401 (m), 1080 (m), 1058 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.67 (d, *J* = 8.6, 1H), 7.10 (d, *J* = 2.2, 1H), 7.00 (dd, *J* = 8.6, 2.2, 1H), 3.88 (s, 3H), 2.06 (q, *J* = 7.5, 2H), 1.72 (s, 3H), 0.92 (t, *J* = 7.5, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 181.2, 163.9, 162.6, 158.6, 121.2, 114.3, 113.1, 112.2, 97.9, 84.2, 55.8, 31.2, 23.4, 8.1. GC/MS *m/z*: 246 (M^+, 52), 217 (100), 203 (74), 175 (36), 119 (17). HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{14}H_{15}O_4^+$, 247.0965; found, 247.0958.

3-Methyl-3-phenylfuro[3,4-b]benzofuran-1(3H)-one (**2e**). Yield: 80.0 mg, starting from 126.6 mg of 2-[(3-hydroxy-3-cyclopentyl)-ethynyl]phenol (57%). Yellow solid, mp = 78−79.0 °C. IR (KBr) ν: 1779 (s), 1613 (w), 1440 (m), 749 (m), 700 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.84−7.78 (m, 1H), 7.64−7.56 (m, 3H), 7.44−7.31 (m, 5H), 2.07 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 181.5, 163.2, 161.8, 138.1, 128.9, 128.8, 126.0, 125.2, 124.9, 121.3, 121.1, 112.8, 111.3, 83.9, 26.8. GC/MS *m/z*: 264 (M^+, 17), 249 (38), 221 (100), 159 (17). HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{13}O_3^+$, 265.0859; found, 265.0862.

3-Isopropylfuro[3,4-b]benzofuran-1(3H)-one (**2g**). Yield: 72.5 mg, starting from 101.0 mg of 2-(3-hydroxy-4-methylpent-1-yn-1-yl)phenol (63%). Yellow solid, mp = 71.0−73 °C. IR (KBr) ν: 1765 (s), 1606 (w), 1281 (m), 954 (m), 765 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.86−7.78 (m, 1H), 7.63−7.55 (m, 1H), 7.46−7.36 (m, 2H), 5.24 (d, *J* = 6.8, 1H), 2.30 (octuplet, *J* = 6.8, 1H), 1.12 (d, *J* = 6.8, 3H), 1.09 (d, *J* = 6.8, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 179.1, 164.3, 161.8, 125.9, 125.1, 121.2, 121.0, 113.6, 112.7, 81.6, 31.5, 17.5, 17.2. GC/MS *m/z*: 216 (M^+, 26), 187 (26), 173 (100), 145 (20). The spectroscopic data agreed with those reported.[7]

2-(Benzofuran-2-yl)butan-2-ol (**3a**). Yield: 5.2 mg, starting from 101.0 mg of 2-(3-hydroxy-3-methylpent-1-yn-1-yl)phenol (5%). Yellow oil. IR (film) ν: 3416 (m, br), 1455 (s), 1374 (w), 1249 (m), 1143 (m), 752 (s) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.54−7.48 (m, 1H), 7.46−7.40 (m, 1H), 7.27−7.15 (m, 2H), 6.56 (d, *J* = 0.9, 1H), 2.37 (s, br, 1H), 1.94 (q, *J* = 7.5, 2H), 1.59 (s, 3H), 0.86 (t, *J* = 7.5, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 162.4, 154.7, 128.3, 123.8, 122.7, 120.9, 111.1, 101.5, 72.3, 34.2, 26.2, 8.4. GC/MS *m/z*: 190 (18), 175 (8), 161 (100), 145 (6). The spectroscopic data agreed with those reported.[18]

2-(Benzofuran-2-yl)propan-2-ol (**3b**). Yield: 8.6 mg, starting from 93.2 mg of 2-(3-hydroxy-3-methylbut-1-yn-1-yl)phenol (9%). Yellow oil. IR (film) ν: 3389 (m, br), 1454 (m), 1253 (s), 1166 (m), 751 (s) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.51 (d, *J* = 7.1, 1H), 7.44 (d, *J* = 7.8, 1H), 7.32−7.12 (m, 2H), 6.55 (s, br, 1H), 2.34 (s, br, 1H), 1.66 (s, 6H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 163.1, 154.7, 128.3, 124.0, 122.7, 121.0, 111.2, 100.3, 69.3, 28.7. GC/MS *m/z*: 176 (M^+, 50), 161 (100), 133 (10), 115 (9). The spectroscopic data agreed with those reported.[19]

1-(Benzofuran-2-yl)cyclopentan-1-ol (**3c**). Yield: 23.7 mg, starting from 107.5 mg of 2-[(1-hydroxycyclopentyl)ethynyl]phenol (22%). Yellow solid, mp = 52−54 °C. IR (KBr) ν: 3278 (m, br), 1454 (m), 1255 (m), 1064 (w), 807 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.53−7.46 (m, 1H), 7.45−7.39 (m, 1H), 7.27−7.14 (m, 2H), 6.57 (d, *J* = 0.8, 1H), 2.32 (s, br, 1H), 2.23−2.06 (m, 2H), 2.05−1.83 (m, 4H), 1.83−1.72 (m, 2H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 162.0, 154.8, 128.4, 123.8, 122.6, 120.8, 111.1, 101.0, 79.9, 39.8, 23.7. GC/MS *m/z*: 202 (M^+, 80), 185 (63), 173 (100), 160 (49), 145 (52), 131 (39). The spectroscopic data agreed with those reported.[20]

2-(6-Methoxybenzofuran-2-yl)butan-2-ol (**3d**). Yield: 11.4 mg, starting from 117.2 mg of 2-(3-hydroxy-3-methylpent-1-yn-1-yl)-5-metoxyphenol (10%). Yellow oil. IR (film) ν: 3430 (m, br), 1618 (m), 1441 (m), 1294 (m), 1147 (m), 824 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.39 (d, *J* = 8.5, 1H), 7.01 (d, *J* = 1.9, 1H), 6.85 (dd, *J* = 8.5, 2.3, 1H), 6.51 (s, br, 1H), 3.84 (s, 3H), 2.09 (s, br, 1H), 1.95 (q, *J* = 7.4, 2H), 1.60 (s, 3H), 0.88 (t, *J* = 7.4, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 161.3, 157.7, 155.6, 121.5, 120.9, 111.6, 101.3, 96.0, 72.3, 55.7, 34.2, 26.1, 8.5; GC/MS *m/z*: 220 (M^+, 21), 202 (73), 191 (100), 187 (72), 175 (7). HRMS (ESI-TOF) *m/z*: $[M-H_2O + H]^+$ calcd for $C_{13}H_{15}O_2^+$, 203.1067; found, 203.1072.

1-(Benzofuran-2-yl)-1-phenylethan-1-ol (**3e**). Yield: 25.7 g, starting from 126.6 mg of 2-[(3-hydroxy-3-cyclopentyl)ethynyl]-phenol (20%). Yellow oil. IR (film) ν: 3409 (m, br), 1453 (s), 1372 (w), 1251 (m), 1066 (w), 751 (m), 700 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.57−7.52 (m, 1H), 7.50−7.44 (m, 2H), 7.44−7.17 (m, 6H), 6.64 (d, *J* = 0.9, 1H), 2.71 (s, br, 1H), 1.97 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 161.4, 154.9, 145.1, 128.3, 128.1, 127.6, 125.3, 124.3, 122.9, 121.2, 111.4, 103.0, 73.4, 29.1. GC/MS *m/z*: 238 (M^+, 33), 223 (100), 195 (21), 145 (39). HRMS (ESI-TOF) *m/z*: $[M-H_2O + H]^+$ calcd for $C_{16}H_{13}O^+$, 221.0961; found, 221.0965.

1-(Benzofuran-2-yl)-1-phenylethan-1-ol (**3f**). Yield: 50.1 mg, starting from 86.2 mg of 2-(3-hydroxybut-1-yn-1-yl)phenol (58%). Yellow oil. IR (film) ν: 3375 (m, br), 1454 (s), 1254 (s), 1076 (m), 806 (m), 752 (s) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.56−7.50 (m, 1H), 7.48−7.42 (m, 1H), 7.30−7.17 (m, 2H), 6.60 (t, *J* = 0.9, 1H), 5.01 (qd, *J* = 6.6, 0.6, 1H), 2.22 (s, br, 1H), 1.63 (d, *J* = 6.6, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 160.2, 154.8, 128.1, 124.2, 122.8, 121.1, 111.2, 101.8, 64.2, 21.4. GC/MS *m/z*: 162 (M^+, 38), 147 (100), 103 (17), 91 (82). The spectroscopic data agreed with those reported.[21]

1-(Benzofuran-2-yl)-2-methylpropan-1-ol (**3g**). Yield: 5.2 mg, starting from 101.0 mg of 2-(3-hydroxy-4-methylpent-1-yn-1-yl)-phenol (5%). Yellow oil. IR (film) ν: 3390 (m, br), 1455 (s), 1254 (m), 1015 (m), 742 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.56−7.49 (m, 1H), 7.44 (d, *J* = 7.9, 1H), 7.30−7.15 (m, 2H), 6.60 (s, 1H), 4.52 (d, *J* = 6.6, 1H), 2.30−2.13 (m, 2H), 1.04 (d, *J* = 6.7, 3H), 0.92 (d, *J* = 6.7, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 158.9, 154.7, 128.1, 123.9, 122.7, 120.9, 111.2, 103.3, 73.8, 33.2, 18.8, 17.9. GC/MS *m/z*: 190 (M^+, 29), 147 (100), 91 (49). HRMS (ESI-TOF) *m/z*: $[M-H_2O + H]^+$ calcd for $C_{12}H_{13}O^+$, 173.0961; found, 173.0958.

General Procedure for the Carbonylative Double Cyclization of 2-(3-Hydroxy-1-yn-1-yl)phenols 1a−e, 1g−1j in $BmimBF_4$ (Table 4). A 250 mL stainless-steel autoclave was charged in the presence of air with PdI_2 (1.9 mg, 5.3×10^{-3} mmol), KI (17.5 mg, 0.105 mmol), DIPEA (130 mg, 1.01 mmol), and compounds **1** (0.53 mmol; 100.8 mg, **1a**; 93.6 mg, **1b**; 107.9, **1c**; 117.0 mg, **1d**; 126.8 mg, **1e**; 101.3 mg, **1g**; 115.0 mg, **1h**; 123.5 mg, **1i**; 136.5 mg, **1j**). $BmimBF_4$ (10.5 mL) was then added, and the autoclave was pressurized with CO (6 atm) and air (up to 30 atm). After stirring at 80 °C for 24 h, the autoclave was cooled and degassed. The mixture was then extracted with Et_2O (6 × 10 mL), and the residue (still containing the catalyst dissolved in the IL) was used as such for the next recycle (see below). The collected ethereal phases were concentrated and the product purified by column chromatography on silica gel to give pure furobenzofurane derivatives **2** (eluent: 99:1 to 9:1 hexane−AcOEt; 92.1 mg, 80%, **2a**; 80.8 mg, 75%, **2b**; 105.6 mg, 87%, **2c**; 102.9 mg, 79%, **2d**; 113.2 mg, 81%, **2e**; 93.1 mg, 81%, **2g**; 106.9 mg, 83%, **2h**; 117.5 mg, 86%, **2i**; 111, 0 mg, 74%, **2j**). The isolated yields obtained in each experiment are given in Table 4.

Recycling Procedure. After removal of Et_2O under vacuum, the residue obtained as described above, still containing the catalyst dissolved in the IL, was transferred into the autoclave. Compounds **1**

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(0.53 mmol) and DIPEA (130 mg, 1.00) were added, and then the same procedure described above was followed.

Carbonylative Double Cyclization of 2-(3-Hydroxy-3-methylpent-1-yn-1-yl)phenol 1a on a Larger Scale (Table 3, entry 8). A 250 mL stainless-steel autoclave was charged in the presence of air with PdI_2 (9.0 mg, 0.025 mmol), KI (83.0 mg, 0.50 mmol), DIPEA (645.0 mg, 4.99 mmol), and 2-(3-hydroxy-3-methylpent-1-yn-1-yl)phenol **1a** (475.1 mg, 2.50 mmol). $BmimBF_4$ (50 mL) was then added, and the autoclave was pressurized with CO (6 atm) and air (up to 30 atm). After stirring at 80 °C for 24 h, the autoclave was cooled and degassed. The mixture was then extracted with Et_2O (6 × 30 mL), the collected ethereal phases were concentrated and the product purified by column chromatography on silica gel (eluent: 99:1 to 9:1 hexane−AcOEt) to give pure 3-ethyl-3-methylfuro[3,4-*b*]benzofuran-1(3*H*)-one (**2a**) (403 mg, 75%).

*1′H-Spiro[cyclohexane-1,3′-furo[3,4-b]benzofuran]-1′-one (**2h**).* Yield: 106.9 mg, starting from 115.0 mg of 2-[(1-Hydroxycyclohexyl)-ethynyl]phenol (83%). Yellow solid, mp = 61−63 °C. IR (KBr) ν: 1768 (s), 1441 (m), 1148 (m), 927 (m), 755 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.89−7.76 (m, 1H), 7.63−7.54 (m, 1H), 7.46−7.34 (m, 2H), 2.05−1.76 (m, 8H), 1.70−1.54 (m, 2H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 183.4, 163.7, 161.3, 125.7, 125.0, 121.1, 112.7, 111.2, 83.5, 34.6, 24.4, 22.4. GC/MS *m*/*z*: 242 (M^+, 99), 214 (46), 199 (36), 171 (100), 147 (60). The spectroscopic data agreed with those reported.[7]

*6′-Methoxy-1′H-spiro[cyclopentane-1,3′-furo[3,4-b]-benzofuran]-1′-one (**2i**).* Yield: 117.5 mg, starting from 123.5 mg of 2-[(1-hydroxycyclopentyl)ethynyl]-5-methoxyphenol (86%). Yellow solid, mp = 103−104 °C. IR (KBr) ν: 1767 (s), 1497 (m), 1273 (w), 1080 (m), 953 (m), 756 (s) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.64 (d, *J* = 8.6, 1H), 7.10 (d, *J* = 2.2, 1H), 6.98 (dd, *J* = 8.6, 2.2, 1H), 3.88 (s, 3H), 2.38−1.85 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 179.8, 163.9, 162.7, 158.6, 121.0, 114.5, 113.0, 111.9, 97.9, 90.5, 55.9, 36.9, 24.7; GC/MS *m*/*z*: 258 (M^+, 78), 230 (24), 214 (27), 201 (25), 189 (100), 174 (48). HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{15}H_{15}O_4^+$, 259.0965; found, 259.0959.

*3-(4-Fluorophenyl)-3-methylfuro[3,4-b]benzofuran]-1(3H)-one (**2j**).* Yield: 111.0 mg, starting from 136.5 mg of 2-[3-(4-fluorophenyl)-3-hydroxybut-1-yn-1-yl]phenol (74%). Yellow solid, mp = 75−77 °C. IR (KBr) ν: 1771 (s), 1443 (m), 1266 (m), 1150 (m), 945 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.85−7.77 (m, 1H), 7.66−7.57 (m, 1H), 7.47−7.30 (m, 5H), 7.11−6.99 (m, 1H), 2.07 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 180.9, 162.9 (d, *J* = 248.0), 162.8, 161.8, 140.6 (d, *J* = 7.4), 130.6 (d, *J* = 8.3), 126.2, 125.3, 121.4, 121.0, 120.6 (d, *J* = 3.3), 115.8 (d, *J* = 21.1), 112.9, 112.4 (d, *J* = 23.6), 111.4, 83.1, 26.8. $^{19}F\{^1H\}$ NMR (471 MHz, $CDCl_3$): −111.6. GC/MS *m*/*z*: 282 (M^+, 28), 267 (43), 239 (100), 183 (14), 159 (30). HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{17}H_{12}FO_3^+$, 283.0765; found, 283.0770.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.9b00952.

Copies of HRMS spectra for all news compounds, and copies of ^1H NMR, $^{13}C\{^1H\}$ NMR, and ^{19}F NMR spectra for all compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: raffaella.mancuso@unical.it (R.M.).
*E-mail: bartolo.gabriele@unical.it (B.G.).

ORCID

Raffaella Mancuso: 0000-0001-7514-6096
Diego Olivieri: 0000-0001-9411-4487
Nicola Della Ca': 0000-0002-7853-7954
Bartolo Gabriele: 0000-0003-4582-1489

Notes

The authors declare no competing financial interest.

■ DEDICATION

Dedicated to the memory of Professor Cinzia Chiappe.

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(8) As we have already observed in many other PdI_2/KI-catalyzed carbonylation processes,[3] the use of KI, besides favoring PdI_2 solubilization, can be beneficial, since it may stabilize the intermediate organometallic complexes leading to the final carbonylated product.

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(10) Interestingly, the same phenomenon was not observed in the conversion of 2-(hydroxypropyn-1-yl)anilines into fused furo[3,4-*b*] indol-1-ones, recently reported by our research group, where the carbonylative double cyclization also took place with substrates bearing a primary or a secondary alcoholic function.[5] However, the substrates used in the present work have a different reactivity with

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respect to 2-(hydroxypropyn-1-yl)anilines; in fact, they need to be deprotonated in situ by the DIPEA base to give a more nucleophilic phenate intermediate before cyclization may occur (Scheme 1 and Table 1, entry 1). This makes them particularly prone to undergo Pd-catalyzed simple cycloisomerization, which leads to undesired byproducts **3** (Scheme 1, path b). Accordingly, in the absence of some effect promoting the carbonylative cyclization step (Scheme 1, path a), such as the reactive rotamer effect exerted by double substitution α to the hydroxyl (or monosubstitution with a bulky group), the cycloisomerization pathway tends to be faster with respect to carbonylative double cyclization, and benzofurans **3** are formed preferentially, as observed for **1f** (Table 2, entry 6).

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