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Photoinduced Synthesis of Dibenzofurans: Intramolecular and Intermolecular Comparative Methodologies

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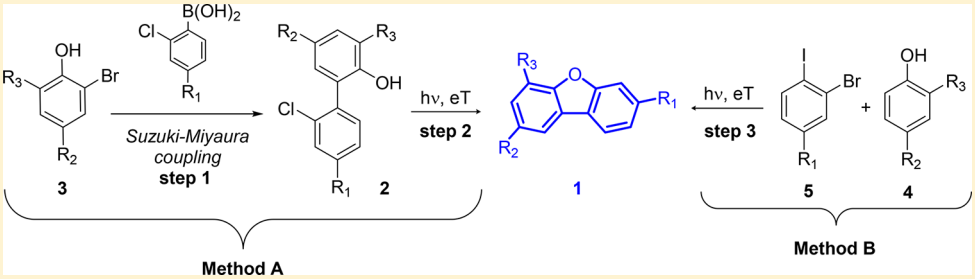
Supporting Information



ABSTRACT: The $S_{RN}1$ reaction has been used as a powerful tool for the synthesis of heterocycles, and only a few studies about photoinduced intramolecular cyclization to generate a new C−O bond by a radical pathway have been reported. This work introduces two strategies for the synthesis of substituted dibenzofurans by electron transfer (eT) reactions. The first one is a three-step process that comprises bromination of *o*-arylphenols, Suzuki−Miyaura cross-coupling and photoinduced cyclization in order to obtain the above-mentioned products. The second one is a metal-free procedure and does not require any photocatalyst. Different solvents were tested, and the yields ranged from low to moderate. A comparison was established between both methodologies, showing that the second one is the most suitable for the synthesis of dibenzofurans.

INTRODUCTION

The dibenzofuran nucleus provides chemical characteristics that enable it to position itself as a versatile molecule in different fields of chemical research. Different potential applications have been studied, such as anticancer,[1,2] antioxidant,[3] antibacterial[4−7] and as enzyme inhibitors.[8,9] In addition, substituted dibenzofurans have been used in the development of OLED.[10]

Due to its promising activity in the development of optoelectronic materials and their intriguing biological properties, in the past decade, the chemical synthetic community has focused on improving the methodologies that allow to access to the substituted dibenzofuran nucleus. The synthetic approaches to prepare dibenzofurans can be classified into two main categories. One involves the construction of the dibenzofuran from diaryl ethers.[11−13] The mechanism proposed for the formation of the new C−C bond proceeds through three sequential steps, in the presence of Pd,[14,15] Rh[16] or Ag.[17]

The second category refers to the intramolecular *o*-arylation of 2-arylphenols. This method is mainly based on the activation of C−H bonds catalyzed by Pd[18−21] or Cu[22] and a subsequent intramolecular etherification. The last step can also be achieved by starting from 2′-halo-arylphenols.[23,24] Moreover, a few examples are reported where dibenzofurans are generated from 2′-halo-arylphenols in metal-free conditions, employing light or high temperatures. An example is the synthesis of naphtho[1,2-*b*]benzofuran, which was reported by photocyclization of 1-(2-chlorophenoxy)naphthalene.[25] Furthermore, intramolecular O-/N-arylations afford dibenzofurans and carbazoles respectively by a typical S_NAr pathway, in the presence of potassium-*tert*-butoxide and high temperatures.[20] Recently, a combination of in situ diazotization and a later photocatalytic process promoted by a photosensitizer was reported for the synthesis of dibenzofurans from 2-(2′-aminoaryl)phenols. These substrates were synthesized previously by C−H bond activation mainly, using metal catalysts as Pd or Ni.[26]

In the last years, a third approach has emerged, in which the synthesis of dibenzofurans is planned from simpler substrates and all together react in a one-pot methodology. This is the case of a Michael-oxidation-oxa-Michael reaction sequence to obtain dibenzo[*b*,*d*]furan scaffolds from the binding of substituted phenols and *o*-benzoquinones.[27] The construction of dibenzofuran from 6-diazo-2-cyclohexenone and *o*-haloiodobenzene in a one-pot synthesis has also been developed. In this case, the process involves two metal-catalyzed cross-coupling reactions.[28]

However, up to now the great majority of the synthetic methods used present drawbacks such as high temperatures, use of transition metals, tedious procedures and extensive reaction times.

On the other hand, radical synthesis has proved to be an advantageous alternative in comparison with other mechanisms

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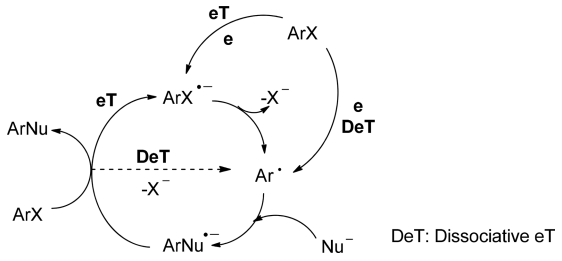
due to shorter reaction times, simpler methodologies and also involves a synthetic route free of heavy metals.[29] In particular, the radical nucleophilic substitution mechanism ($S_{RN}1$) is a chain process that involves radicals and radical anions as intermediates.[30,31] The initiation step is an electron transfer (eT) from a suitable donor (e.g., the nucleophile) to afford the radical anion of the substrate $(ArX)^{\bullet-}$ as shown in Scheme 1.

Scheme 1. $S_{RN}1$ Mechanism



This process can be induced by light, inorganic salts, electrochemically, by solvated electrons or thermally (spontaneous reactions). The $S_{RN}1$ mechanism offers the possibility of achieving substitution in compounds that are nonreactive under classical nucleophilic substitutions, is also compatible with many substituents, and in addition, several nucleophiles such as carbanions and heteroatomic anions can be used to form new C−C or C−heteroatom bonds with good yields, respectively. The scope of this process has increased considerably and currently serves as an important synthetic route for different types of compounds.[30,31]

The $S_{RN}1$ mechanism has clearly manifested to be useful for obtaining heterocyclic compounds.[32] Recently, the $S_{RN}1$ reaction was applied to form new C−C bonds in the synthesis of heterocycles such as phenanthridines and benzophenanthridines,[33] phenanthrolines,[34] 1-phenyl-1-oxazolyl-Indane derivatives,[35] cyclopenta-oxazolo-isoquinolin-6-ones[36] carbazoles and carbolines,[37,38] pyrrole, indole, and pyrazole fused azaheterocycles.[39] The formation of C-heteroatom bonds is also reported as a consequence of an intramolecular cyclization to generate compounds such as 9*H*-carbazoles,[40] among others. Although, the intramolecular reaction $S_{RN}1$ has been shown to be a powerful tool for the synthesis of heterocycles, only few reports about photoinduced intramolecular cyclization to generate a new C−O bond by a radical pathway have been found. Benzoxazoles from pyrrole-2-carboxamide or indole-2-carboxamide,[41] naphtho[2,1-*b*]benzofurans from the photostimulated reaction between *o*-bromoiodobenzene and the 2-naphthoxide ion[42] and phenanthro[9,10-*b*]benzofuran from the *o*-dihalobenzene and the anion of phenanthren-9-ol.[43]

Therefore, we were interested in developing a complementary approach to have access to the dibenzofuran framework by photostimulated eT reactions. Two synthetic pathways were studied to obtain the same substituted dibenzofuran. In the first one, substituted *o*-arylphenols were used and, in the second pathway, substituted phenols and *o*-dihalobenzene react in a one-pot method for the synthesis of dibenzofurans.

In the present work we first carried out the construction of 2′-chloro-3-R_3-5-R_2-[1,1′-biphenyl]-2-ol (**2**, R: substituent), which both, leaving group and nucleophile, are located within the same molecule (step 1, Method A in Scheme 2). In a second phase, the formation of a new C−O bond by a photoinduced intramolecular reaction of **2**, to give the corresponding substituted dibenzofurans (**1**) was studied as a key step (step 2, Method A in Scheme 2). On the other hand, the development of a one-pot methodology involving the photoinduced $S_{RN}1$ process to obtain **1** was also studied. This is the reaction between 2-bromo-1-iodo-4-R_1benzene (**5**) and the substituted phenol **4** (step 3, Method B in Scheme 2).

RESULTS AND DISCUSSION

Method A. *1. Synthesis of Substituted 2′-Chloro-3-R_3-5-R_2-[1,1′-biphenyl]-2-ol (2) Compounds (Step 1, Method A).* Substituted 2-halo-phenylphenols were prepared by a cross-coupling Suzuki−Miyaura reaction[44−46] from 2-chlorophenylboronic acid and *p*-substituted *o*-brominated phenols (**3**) as substrates. Compounds **2a−d** were synthesized employing PPh_3 as ligand[47−49] and a palladium source such as $Pd(OAc)_2$ or $Pd(dba)_2$. Instead, Pd/C was used for the synthesis of compounds **2e−h** and no ligand was taken into account (Table 1). It is noteworthy that several reaction conditions were carried out changing the solvent, ligands or bases with the objective of improving yields of the Suzuki−Miyaura cross coupling products (Scheme 3).

Regardless of the methodology used, 2,2′-dichloro-1,1′-biphenyl was observed as a byproduct from the homocoupling of boronic acid.[1,52] *o*-Bromophenols with electron withdrawing groups (EWG) as substituents, such as **3d** and **3g** (Table 1, entries 4 and 7), gave the lowest yields of this set of reactions, **2d** and **2g** respectively.

On the other hand, substituted phenols with electron donating groups (EDG) showed better yields such as products **2b** and **2e** (Table 1, entries 2 and 5). The exceptions are products **2c** and **2f**, which were obtained with low yields.

In many cases, the electronic effects have been used to rationalize different reactivity of haloarenes in cross-coupling reactions, such as the Suzuki−Miyaura one, which is important for the regioselective transformations of polyhalogenated aromatic compounds.[53−56] On the other hand, Fauvarque et al.[57] proposed an analogy between aromatic nucleophilic substitution (S_NAr) and the oxidative addition of transition

Scheme 2. Synthesis of Substituted Dibenzofurans by Electron Transfer Reactions

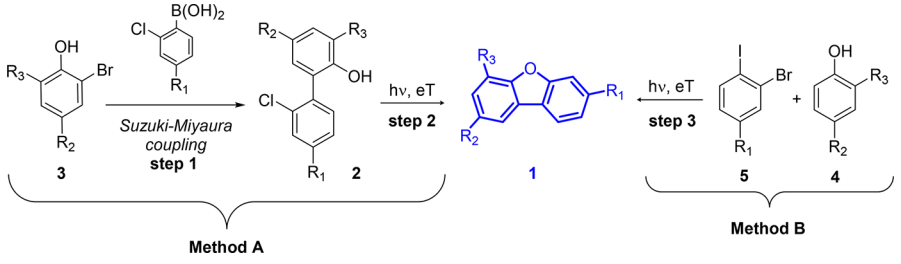


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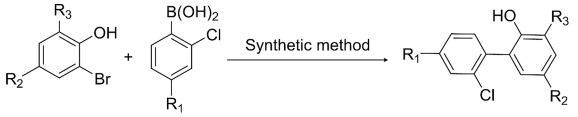
Table 1. Suzuki–Miyaura Cross-Coupling Reactions for the Synthesis of Substituted 2′-Chloro-3-R_3-5-R_2-[1,1′-biphenyl]-2-ol (2)[a]

entry	3	method		time (h)	2 (% isolated yield)
		Method with Pd-PPh_3[b]			
		Pd (%)	PPh_3 (%)		
1	**3a**[c] (R_2 = R_3 = H)	2 $Pd(OAc)_2$	4	0.25	**2a** (58)
2	**3b** (R_2 = CH_3, R_3 = H)	15 $Pd(OAc)_2$	30	0.5	**2b** (67)
3	**3c** (R_2 = OCH_3, R_3 = H)	5 $Pd(dba)_2$	10	0.5	**2c** (15)
4	**3d** (R_2 = F, R_3 = H)	5 $Pd(dba)_2$	10	0.5	**2d** (10)
		Method with Pd/C[d]			
		Pd/C (%)	CsF (equiv)		
5	**3e** (R_2 = $C(CH_3)_3$, R_3 = H)	2	4	2.5	**2e** (40)
6	**3f** (R_2 = R_3 = $C(CH_3)_3$)	6	12	120	**2f** (20)
7	**3g** (R_2 = CN, R_3 = H)	10	4	3	**2g** (<10)
8	**3b**[e] (R_2 = CH_3, R_3 = H)	10	4	3	**2h** (25)

[a]Ratio of **3**:chlorophenylboronic acid was 1:1.3. Isolated yields are given in parentheses. [b]For the method A: solvent dioxane:H_2O mixture in 4:1 ratio and 3 equiv of K_3PO_4 were added. Heating was performed by MW[50,51] at 150 °C for the specific time in atmosphere of N_2. [c]1 equiv of *o*-iodophenol was used as substrate. [d]For the method B: solvent H_2O (5 mL). It was used a 6% of NBu_4Br. T = 80 °C. [e]It was used 2-chloro-4-methylphenylboronic acid (R_1 = CH_3).

Scheme 3. Representation of the Suzuki–Miyaura Cross-Coupling Reaction between Substituted *o*-Bromophenols (3) and *o*-Chlorophenylboronic Acids



3

3a (R_2= R_3= H)
3b (R_2= CH_3; R_3= H)
3c (R_2= OCH_3; R_3= H)
3d (R_2= F; R_3= H)
3e (R_2= $C(CH_3)_3$; R_3= H)
3f (R_2= R_3= $C(CH_3)_3$)
3g (R_2= CN; R_3= H)
3b (R_2= CH_3; R_3= H)

2

2a (R_1= R_2= R_3=H)
2b (R_1= H, R_2= CH_3, R_3= H)
2c (R_1= H, R_2= OCH_3, R_3= H)
2d (R_1= H, R_2= F, R_3= H)
2e (R_1= H, R_2= $C(CH_3)_3$, R_3= H)
2f (R_1= H, R_2= R_3= $C(CH_3)_3$)
2g (R_1= H, R_2= CN, R_3= H)
2h (R_1= CH_3, R_2= CH_3; R_3= H)

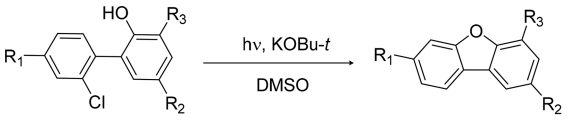
metals to the C-halogen bond of haloarenes. They postulated that brominated phenols would behave as nucleophiles, and that their performance would be determined by the inductive effect, charge effect or steric hindrance that each substituent could contribute on the molecule.

For the phenol **3c**, the presence of the methoxy group could generate an inductive effect on the molecule, converting it into a deficient substrate (analogy with a weak nucleophile) to the oxidative addition step with palladium. Otherwise, the presence of the two *t*-butyl groups in **3f**, would generate a difficulty to the oxidative addition step by steric hindrance, decreasing the yield of **2f**.

Product **2g** was evidenced by GC–MS in the reaction mixture. It was isolated in very low quantity, enough just to characterize it by NMR.

2. Synthesis of Substituted Dibenzofurans (1) by Photoinduced Intramolecular Reaction (Step 2, Method A). The substrates (**2a–h**) were then engaged in the $S_{RN}1$ reaction in order to achieve the synthesis of the substituted dibenzofurans was further explored (Scheme 4). The results are presented in Table 2.

Scheme 4. Photostimulated Intramolecular Reaction of Substituted 2′-Chloro-[1,1′-biphenyl]-2-ols (2)



2

2a (R_1= R_2= R_3= H)
2b (R_1= H, R_2= CH_3, R_3= H)
2c (R_1= H, R_2= OCH_3, R_3= H)
2d (R_1= H, R_2= F, R_3= H)
2e (R_1= H, R_2= $C(CH_3)_3$, R_3= H)
2f (R_1= H, R_2= R_3= $C(CH_3)_3$)
2h (R_1= R_2= CH_3, R_3= H)

1

1a (R_1= R_2= R_3= H)
1b (R_1= H, R_2= CH_3, R_3= H)
1c (R_1= H, R_2= OCH_3, R_3= H)
1d (R_1= H, R_2= F, R_3= H)
1e (R_1= H, R_2= $C(CH_3)_3$, R_3= H)
1f (R_1= H, R_2= R_3= $C(CH_3)_3$)
1h (R_1= R_2= CH_3, R_3= H)

Table 2. Photostimulated Intramolecular Reaction of Substituted 2′-Chloro-[1,1′-biphenyl]-2-ol (2) in DMSO[a]

entry	2	1 (% isolated yield)	conversion (%)
1[b]	**2a** (R_1 = R_2 = R_3 = H)	**1a** (89)	93
2	**2a** (R_1 = R_2 = R_3 = H)	**1a** (84)	88
3[c]	**2a** (R_1 = R_2 = R_3 = H)	**1a** (38)	55
4[d]	**2a** (R_1 = R_2 = R_3 = H)	**1a** –	–
5[e]	**2a** (R_1 = R_2 = R_3 = H)	**1a** –	–
6[f]	**2a** (R_1 = R_2 = R_3 = H)	**1a** (53)	60
7	**2b** (R_1 = H, R_2 = CH_3, R_3 = H)	**1b** (51)	90
8	**2c** (R_1 = H, R_2 = OCH_3, R_3 = H)	**1c** (49)	73
9	**2d** (R_1 = H, R_2 = F, R_3 = H)	**1d** (60)	92
10	**2e** (R_1 = H, R_2 = $C(CH_3)_3$, R_3 = H)	**1e** (67)	84
11	**2f** (R_1 = H, R_2 = R_3 = $C(CH_3)_3$)	**1f** (50)	84
12	**2h** (R_1 = R_2 = CH_3, R_3 = H)	**1h** (78)	79

[a][**2**] = 50 mM, [KOBu-*t*] = 0.1 M. Irradiation time = 3 h, N_2 atmosphere. Conversion was determined potentiometrically by titration of chloride anions with $AgNO_3$. [b]The reaction was carried out in 60 mL of $NH_3(l)$ (−33 °C), [**2a**] = 4 mM, [KOBu-*t*] = 8 mM. [c]Irradiation time = 2 h. [d]Absence of light. [e]In the absence of KOBu-*t*. [f]Addition of 30 mol % of *m*-DNB respect to **2a**.

After 180 min of irradiation, the reaction of 2′-chloro-[1,1′-bifenil]-2-ol (**1a**) in liquid ammonia with excess of KOBu-*t* (2 equiv) afforded the dibenzofuran (**1a**) in 89% yield (Table 2, entry 1). A similar result was obtained in DMSO as solvent (Table 2, entry 2). As the yields of **1a** have no significant difference with the change of the solvent, DMSO was preferred to simplify the experimental setup.

Monosubstituted and disubstituted dibenzofurans **1b–h** were obtained in moderate to good yields using **2b–2h**. Quantification of chloride ion informs about the conversion of the substrate. The reduced product was evidenced only in traces in some of the reactions, which is obtained from the hydrogen atom abstraction by the radical (**2a**$^{\bullet}$), usually from the solvent. In general, the conversions are very good for all substrates studied.

There was no reaction under dark conditions (in absence of light), which excludes a benzyne mechanism (Table 2, entry 4). The effect of the base was evaluated by carrying out the

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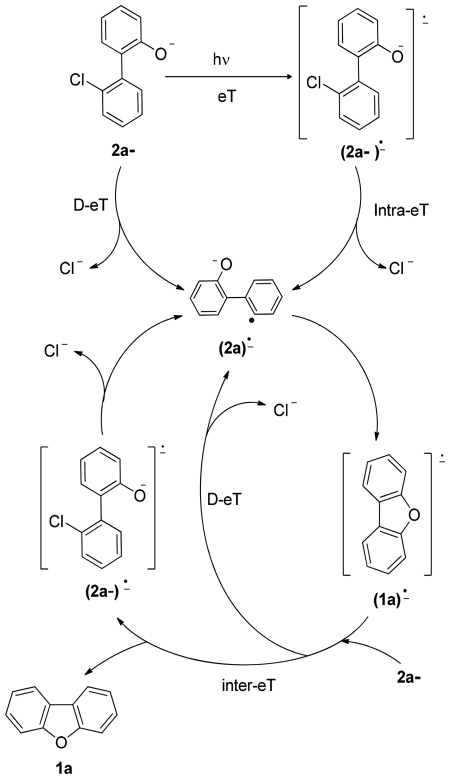
photostimulated reaction in the absence of KOBu-*t* (Table 2, entry 5) and no product **2a** was observed. It is necessary to have the anion form of the substrate for the mechanism success. Also, the photostimulated reaction was partially inhibited when adding 30 mol % of *m*-dinitrobenzene (*m*-DNB), a strong electron-acceptor (Table 2, entry 6), which would indicate the presence of radical anions in the reaction mechanism.

The results suggest that the formation of the new C−O bond occurs through eT reactions with radicals and radical anions as intermediates. The formation of the dibenzofuran **1a** via the nucleophilic radical substitution mechanism $S_{RN}1$ (Scheme 5).

Scheme 5. Mechanism Proposed for the Synthesis of Dibenzofuran 1a by a Photoinduced Intramolecular $S_{RN}1$ Reaction

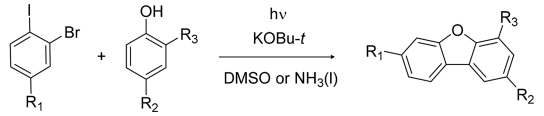


Method B. *Synthesis of Substituted Dibenzofurans by Photoinduced Intermolecular Reaction.* In order to explore deeper the synthesis of dibenzofurans by reactions that are free of heavy metals, a one-pot methodology was proposed to obtain substituted dibenzofurans following a bimolecular coupling between *p*-substituted phenols and 2-bromo-1-iodo-4-R_1benzene under $S_{RN}1$ conditions (Scheme 6).

The reaction conditions and optimization were explored with **4e** as a model substrate.[58] When reaction of **4e** with 2-bromoiodobenzene (**5a**) was carried out for 3 h, in liquid ammonia as solvent, the corresponding dibenzofuran **1e** (15% yield) was obtained. When the irradiation time has increased to 6 h, the yield of **1e** was improved (55%, Table 3, entry 5). Both results obtained for the yield of **1e** are similar in DMSO and $NH_{3(l)}$, 52% and 55% respectively, (Table 3, entries 1 and 5).

Aromatic or benzyne mechanisms were discarded because no reaction took place in absence of light. The yield of **1e** was lower when 30 mol % of *m*-DNB was added (18%, Table 3, entries 2 and 4) suggesting the participation of radical anions as

Scheme 6. Synthesis of Substituted Dibenzofurans (1) by Photostimulated Nucleophilic Substitution of 2-Bromo-1-iodo-4-R_1benzene (5) with Substituted Phenols (4)



5a (R_1= H)	**4a** (R_2=R_3= H)	**1a** (R_1= R_2= R_3= H)
	4b (R_2= CH_3, R_3= H)	**1b** (R_1= H, R_2= CH_3, R_3= H)
	4c (R_2= OCH_3, R_3= H)	**1c** (R_1= H, R_2= OCH_3, R_3= H)
	4d (R_2= F, R_3= H)	**1d** (R_1= H, R_2= F, R_3= H)
	4e (R_2= $C(CH_3)_3$, R_3= H)	**1e** (R_1= H, R_2= $C(CH_3)_3$, R_3= H)
	4f (R_2= R_3= $C(CH_3)_3$)	**1f** (R_1= H, R_2= R_3= $C(CH_3)_3$)
	4g (R_2= CN, R_3= H)	**1g** (R_1= H, R_2= CN, R_3= H)
	4i (R_2= R_3= CH_3)	**1i** (R_1= H, R_2= R_3= CH_3)
5b (R_1=CH_3)	**4d** (R_2= F, R_3= H)	**1j** (R_1= CH_3, R_2= F, R_3= H)
	4e (R_2= $C(CH_3)_3$, R_3= H)	**1k** (R_1= CH_3, R_2= $C(CH_3)_3$, R_3= H)
5c (R_1=OCF_3)	**4c** (R_2= OCH_3, R_3= H)	**1l** (R_1= OCF_3, R_2= OCH_3, R_3= H)

intermediates. These last experiments are good evidence of a $S_{RN}1$ type mechanism.

The mechanism proposed for the synthesis of products **1** by the bimolecular pathway is shown in Scheme 7. As can be seen, the 2-bromophenyl radical generated in step 1′ may couple at the *ortho*-C respecting to the C−O bond of the substituted phenolate ion to finally generate the monosubstituted product with retention of the bromine atom **6** (step 2′). On the other hand, fragmentation of the C−Br bond by intramolecular eT (intra-eT) and later deprotonation affords the radical anion intermediate $\mathbf{2}^{\bullet-}$, which by an intramolecular cyclization finally produces the substituted dibenzofuran **1** (step 3′).

The aim to extend this one-pot methodology for the synthesis of monosubstituted dibenzofurans was evaluated using different *p*-substituted phenols (**4**) with 2-bromo-1-iodobenzene (**5a**), (Table 3, entry 5−9 and 11). The yields ranged from low to moderate. It was observed that reactions with phenols **4d** and **4g**, having a EWG as substituent, give lower yields of their products **1d** and **1g** respectively, than the phenols with EDG substituents employed. This is in agreement with previous studies where it was shown that, under electrochemical or photostimulated initiation, the substitution yields on arylated substrates increase when the phenoxy ion has electron donor groups as substituents such as *p*-OCH_3 or 2,4-di-$C(CH_3)_3$.[59−62]

In the same way, it can be assumed that EWG located at the *para* position in the phenol generates a lower reactivity of the phenoxy anion by converting it into a less reactive nucleophile. For this type of phenols, the coupling reaction between the nucleophile and the substrate radical and the eT from the radical anion of the substitution product toward the substrate become the crucial steps. When these steps are not efficient, the chain will be short or even nonexistent and the scope of substitution will fail.[30] Therefore, for these cases it is necessary that the chain restarts constantly; which means longer irradiation times. This was also observed experimentally, products **1d** and **1g** required higher times of photostimulation.

The quantification of I^- indicates the generation of the radical anion of substrate **5a** and its subsequent mesolytic fragmentation and it seems to be efficient under this methodology. This is also confirmed because the main byproducts found were benzene and bromobenzene for all reactions (compounds resulting from H atom abstraction).

The monosubstitution compound with the second halogen retention was not observed as a byproduct, except in the reaction of phenol **4d** (traces) and **4g**. For this last particular

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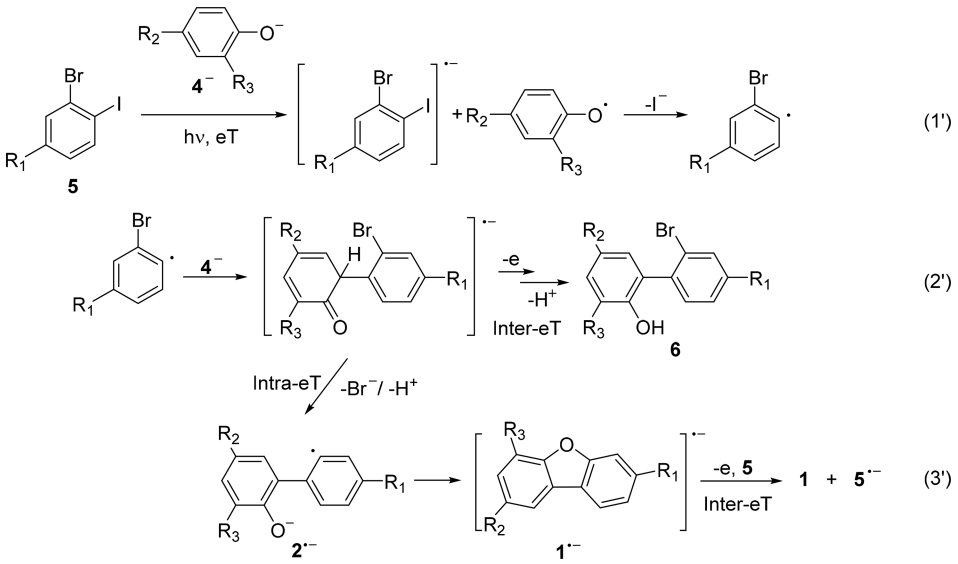
Table 3. Photostimulated Nucleophilic Substitution of *p*-Substituted Phenols (4) with 2-Bromo-1-iodo-4-R_1benzene (5)[a]

Entry	5	4	Reaction time (h)	1 (% isolated yield)	I^- (%)	Br^- (%)
1	**5a** (R_1 = H)	**4e** (R_2= $C(CH_3)_3$, R_3= H)	6	**1e** (52)	75	69
2[b]		**4e** (R_2= $C(CH_3)_3$, R_3= H)	6	--	--	--
3[c]		**4e** (R_2= $C(CH_3)_3$, R_3= H)	6	--	--	--
4[d]		**4e** (R_2= $C(CH_3)_3$, R_3=H)	2	**1e** (18)	77	20
5[e]		**4e** (R_2= $C(CH_3)_3$, R_3= H)	6	**1e** (55)	79	76
6[f]		**4a** (R_2= R_3= H)	4	**1a** (20)	93	74
7		**4b** (R_2= CH_3, R_3= H)	6	**1b** (57)	88	69
8		**4c** (R_2= OCH_3, R_3= H)	4	**1c** (40)	99	96
9		**4d** (R_2= F, R_3=H)	7	**1d** (15)	20	15
10		**4f** (R_2= R_3= $C(CH_3)_3$)	6	**1f** (40)	98	70
11		**4g** (R_2= CN, R_3= H)	8	**1g** (31)	65	32
12		**4i** (R_2= R_3= CH_3)	6	**1i** (47)	92	49
13[e]	**5b** (R_1 = CH_3)	**4d** (R_2= F, R_3= H)	6	**1j** (64)	99	92
14		**4e** (R_2= $C(CH_3)_3$, R_3= H)	6	**1k** (43)	87	80
15[e]	**5c** (R_1 = OCF_3)	**4c** (R_2= OCH_3, R_3= H)	6	**1l** (48)	81	54

[a][5] = 50 mM, [4] = 0.15 M, [KOBu-*t*] = 0.15 M, N_2 atmosphere. Halide ions were determined potentiometrically by titration with $AgNO_3$. Bromobenzene, benzene and 2-bromoiodobenzene were found as byproducts but they were not quantified. [b]Absence of light. [c]In the absence of KOBu-*t*. [d]30 mol % of *m*-DNB was added. [e]$NH_3(l)$ as solvent, [5] = 2 mM, [4] = 6 mM, [KOBu-*t*] = 6 mM. [f]Traces of [1,1′-biphenyl]-4-ol was detected by GC−MS.

Scheme 7. Mechanism Proposed To Obtain Dibenzofurans by a Bimolecular Mechanism Type $S_{RN}1$



case, **1g** and **6g** were found as reaction products. This can be explained by an intermolecular eT after the first substitution (step 2′, Scheme 7) competing with the intramolecular eT to give the final cyclized product (step 3′, Scheme 7). The ratio between monosubstituted and cyclized product depends on the relative rate constants for both intra-eT and inter-eT pathways.[30,63] It was observed the 2′-bromo-6-hydroxy-[1,1′-biphenyl]-3-carbonitrile (**6g**) compound as an intermediate in the formation of the cyclized product **1g** (Scheme 8).[64]

By the other hand, the intra-eT could also occur simultaneously and lead to the formation of **1g** through the intermediary of $(\mathbf{2g})^{\bullet-}$.

Phenols **4f** and **4i** generate disubstituted dibenzofurans **1f** and **1i** in moderate yields, 40 and 47% respectively. Moreover, the disubstitution in the dibenzofuran can be in both aromatic rings by changing the substrate to a substituted *o*-dihalobenzene. Dibenzofurans **1j−l** were obtained in moderate yields following the same experimental procedure, from substrates **5b** and **5c** (Table 3, entries 13−15). The versatility of this methodology is also demonstrated by the use of an *o*-

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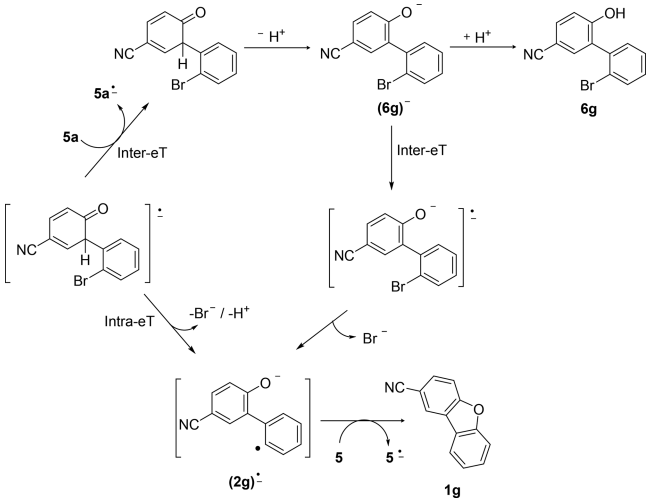
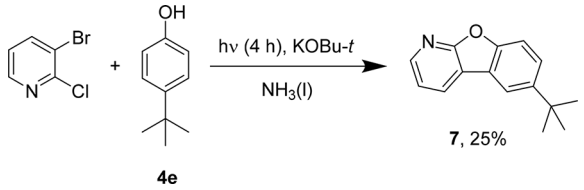
Scheme 8. Mechanism Proposed for the Formation of the Compound Dibenzo[*b*,*d*]furan-2-carbonitrile 1g



dihaloheterocycle as substrate. 6-(*tert*-Butyl)benzofuro[2,3-*b*]-pyridine (**7**) was obtained in 25% isolated yield when the reaction between 3-bromo-2-chloropyridine and 4-(*tert*-butyl)-phenol (**4e**) was carried out as shown in Scheme 9.

Scheme 9. Synthesis of 6-(*tert*-Butyl)benzofuro[2,3-*b*]pyridine (7) by Photostimulated Nucleophilic Substitution of 3-Bromo-2-chloropyridine with 4e



Finally, a comparison of the yields, for the substituted dibenzofurans synthesized by eT reactions in a one-pot methodology (bimolecular reactions from *p*-substituted phenols) and those obtained from the methodology involving Suzuki–Miyaura reactions plus intramolecular eT reactions, are presented in Table 4.

Table 4. Dibenzofuran Yields from the Two Different Pathways

entry	1	total yield of **1** from 2′-chloro-[1,1′-biphenyl]-2-ols synthesis plus photoinduced eT cyclization (%)	yield of the one-pot bimolecular eT reactions (%)
1	**1a**	49	20
2	**1b**	34	57
3	**1c**	7	40
4	**1d**	6	15
5	**1e**	27	52
6	**1f**	10	40
7	**1g**	–	31
8	**1h**	20	–
9	**1i**	–	47
10	**1j**	–	64
11	**1k**	–	43
12	**1l**	–	48

It is clear from Table 4 that global yields of the Suzuki-$S_{RN}1$ reactions are lower than the yields of the one-pot pathway, with exception of product **1a**. In general, the synthesis of 2′-chloro-[1,1′-biphenyl]-2-ols presented several experimental difficulties, mainly due to the presence of the unprotected hydroxyl group. Also, each Suzuki–Miyaura reaction that was carried out, showed different behavior among the phenols used, so it was impossible to make only one procedure for all phenols employed. On the other hand, the bimolecular synthesis pathway is metal-free and, in general, does not have big changes in the experimental conditions; only irradiation time and solvent ($NH_3(l)$ or DMSO) were the parameters to be considered. The same behavior was observed for the reactions when substrates **5b** and **5c** were employed.

■ CONCLUSIONS

This work has developed a novel one-pot strategy for the synthesis of substituted dibenzofurans by eT reactions. The one-pot synthetic route, which is free of transition metals, is carried out from commercial reagents, such as *p*-substituted phenols and 2-bromoiodobenzene, under photostimulated conditions and exhibits moderate yields, but they are very good considering those substituted dibenzofurans obtained from procedures that use photocatalyzers or transition metals. Moreover, the bimolecular procedure is a more efficient option than the pathway involving Suzuki–Miyaura coupling reactions for the formation of halogenated aryl phenols as substrates and then the intramolecular photoinduced eT reaction. Compounds as 2-methyldibenzo[*b*,*d*]furan (**1b**), 2-methoxydibenzo[*b*,*d*]-furan (**1c**) and 2-fluorodibenzo[*b*,*d*]furan (**1d**) are examples of the efficiency of the one-pot synthesis, since they were obtained in similar yields to those reported recently.[26] This methodology shows the versatility of the reaction to obtain a wide range of substituted dibenzofurans. Different substituents could be present in *p*-substituted phenols and/or substituted *o*-dihalobenzenes. This point was demonstrated by the synthesis of 5 novel dibenzofurans (**1f**, **1i**, **1j**, **1k** and **1l**).

■ EXPERIMENTAL SECTION

Phenols, KOBu-*t*, boronic acids, dimethoxyethane, NBS, acetonitrile, ammonium acetate, palladium(II) acetate, $Pd(dba)_2$, triphenylphosphine, bases used in Suzuki–Miyaura reactions, 2-bromoiodobenzene and 3-bromo-2-chloropyridine were obtained from Sigma-Aldrich and used as received. 2-bromo-1-iodo-4-methylbenzene (**5b**) and 2-bromo-1-iodo-4-(trifluoromethoxy)benzene (**5c**) were synthesized from their respective *o*-bromoaniline derivatives following the procedure of the Sandmeyer reaction.[65] Dimethylformamide and dimethyl sulfoxide are Carlo Erba and were stored under molecular sieves (4 Å). Dimethoxyethane (Aldrich) was used as received. Photoirradiation was performed in a reactor equipped with two 400 W lamps (Philips model Master HPI-T Plus, air- and water-cooled). The Figure S1 in SI shows the spectrum of the lamps. Microwave monomode CEM-Discovery reactor was employed for Suzuki–Miyaura reactions showed in Table 1 described by method A. Reactions were performed in a single mode instrument equipped with a noncontact infrared temperature sensor, direct pressure control system for measuring the pressure of the reaction sealed vessel contents and a cooling system by compressed air. The sample vessels reach the selected temperature in about 30 s. Although, the maximum microwave power was set at 150 W, after the initial heating pulse of maximum 100 W for 30 s, the average applied power was about 1 W to keep the selected temperature. After 10 min of irradiation the device cooled the tube to 50 °C with compressed air above 1 min. The average pressure in the vessel was 1.7 atm during the reaction time. After completion of the reaction, the vessel was removed from the microwave cavity and

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opened to the atmosphere for extraction of the crude. HPLC analysis were carried out on a Waters 1525 Binary HPLC Pump connected to a Waters 2998 Photodiodo Array Detector, and employing an Agilent Zorbax Eclipse XDB-C18 Analytical column (4.6 × 150 mm, 5 μm) and Rx-Sil Analytical column (4.6 × 150 mm, 5 μm). Gas chromatographic analysis was performed on a Varian GC with a flame ionization detector, and equipped with a VF-5 ms, 30 m x 0.25 mm × 0.25 mm column. ^{1}H NMR and ^{13}C NMR were recorded on a 400 MHz Bruker nuclear magnetic resonance spectrometer. HRMS were recorded on a Bruker, MicroTOF Q II equipment, operated with an ESI source in (positive/negative) mode, using nitrogen as nebulizing and drying gas and sodium formiate 10 mM as internal standard. Gas Chromatographic/Mass Spectrometer analysis were carried out on a Shimadzu GC−MS QP 5050 spectrometer equipped with a VF-5 ms, 30 m × 0.25 mm × 0.25 mm column. Potentiometric titration of halide ions was performed with a pH meter (Orion) using an Ag/AgCl electrode.

General Procedures for the Synthesis of Brominated Phenols (3a−g). The synthesis of *p*-R-*o*-bromophenols was carried out following different procedures and they were slightly modified.[66−68] The bromophenols were identified by GC−MS.

*Synthesis of **3b**, **3f** and **3g**.* Three mL of acetonitrile and 1 mmol of a corresponding phenol (**4b**, **4f** and **4g**) were added to a 25 mL round-bottomed flask with a magnetic stirrer. After a few minutes, 0.1 equiv of CH_3COONH_4 was added to the mixture. Finally, a solution of 1.05 equiv of NBS dissolved in 2 mL of acetonitrile was added. It was stirred until no substrate was observed. **3b**: 55% yield (102.3 mg), **3f**: 58% yield (165 mg) and **3g**: 60% yield (118 mg).

*Synthesis of **3c** and **3d**.* The reaction was carried out under inert atmosphere. The phenol (1 mmol, **4c** and **4d**) was dissolved in 4 mL of acetonitrile and cooled to 0 °C. The NBS solution (1.05 equiv of NBS dissolved in 2 mL of CH_3CN) was added dropwise. After total addition of NBS, the mixture was stirred at room temperature until total conversion of the phenol. **3c**: 64% yield (129 mg) and **3d**: 70% yield (133 mg).

*Synthesis of **3e**.* The reaction was carried out under inert atmosphere. The phenol (1 mmol, **4e** and **4h**) was dissolved in 1 mL of acetonitrile and cooled to −20 °C. CF_3SO_3H (1.2 equiv) was added to the mixture and, then, a NBS solution (1.05 equiv of NBS dissolved in 2 mL of CH_3CN) was also added, both dropwise. After total addition of NBS, the mixture was stirred at room temperature until total conversion of the phenol. **3e**: 76% yield (173 mg).

For all the methodologies described above, the reactions were quenched by addition of $NaHCO_3$ to reach a pH = 7. Extractions were carried out employing CH_2Cl_2 and H_2O (×3). The organic extracts were dried with Na_2SO_4, filtered, and evaporated under reduced pressure. The crudes were analyzed by GC−MS and the products were purified by column chromatography using as eluent pentane/ethyl acetate (80/20).

General Procedures for the Synthesis of 2′-Chloro-3-R$_2$-5-R$_1$-[1,1′-biphenyl]-2-ol (2). Method with Pd-PPh_3 (synthesis of **2a−d**): Palladium(II) acetate or $Pd(dba)_2$, triphenylphosphine (the equivalents and Pd source are shown in Table 1) and 4 mL of dioxane were added to a microwave sealed tube and stirred for 10 min. Then, the corresponding brominated phenol (1 equiv, 1 mmol), 2-chlorophenylboronic acid (1.5 equiv, 1.5 mmol), K_3PO_4 (3 equiv, 3 mmol) and 1 mL of water were added. The tube was sealed and irradiated in the MW oven at 150 °C for 15 min.

Method with Pd/C (synthesis of **2e−h**): brominated phenol (1 equiv, 0.25 mmol) and 2-chlorophenylboronic acid (1.1 equiv, 0.275 mmol) were added to a Schlenk tube with 5 mL of distilled water. Then, $(n\text{-Bu})_4N^+Br^-$ (6% equiv), CsF, and Pd/C (the equivalents used are indicated in Table 1) were added to the mixture and stirred for the time indicated in Table 1. The system was heated to 80 °C.

Products were first identified by GC and GC−MS. Isolated by column chromatography using pentane and ethyl acetate. **2d** and **2c** were isolated by semipreparative reversed-phase HPLC using acetonitrile and water as HPLC grade eluents.

General Procedure for Photostimulated Intramolecular Reaction of Compounds 2. A solution of compound **2** (1 equiv, 0.245 mmol) and KOBu-*t* (2 equiv, 0.5 mmol) in DMSO (5 mL) is stirred in a previously vacuum-dried Schlenk tube, under N_2 atmosphere. The mixture is irradiated under UV light for 3 h, then quenched by the addition of NH_4NO_3 and deionized water. In dark reactions (without irradiation), the reaction flask was protected from light with aluminum foil and kept under N_2 atmosphere. For the extraction process, CH_2Cl_2 (3 × 20 mL) was used. The organic extract was washed until no residual of DMSO remained, then dried with Na_2SO_4, filtered, and evaporated under reduced pressure.

General Procedure for the Synthesis of Substituted Dibenzofurans by Photoinduced Intermolecular Reaction of Phenols (4) and Substrates (5). Into a previously dried 20 mL Schlenk-type flask (Pyrex) equipped with nitrogen inlet and magnetic stirrer, 7 mL of dried DMSO stored under molecular sieves (4 Å) was added. The solvent was degassed three times under vacuum and stirring, interspersed with N_2. Afterward, KOBu-*t* (3.3 equiv, 1.2 mmol) and the corresponding phenol (3 equiv, 1 mmol) were added. Five minutes later, substrate (**5**) (1 equiv, 0.35 mmol) was added. The mixture was irradiated for 180 min then quenched by the addition of NH_4NO_3, and deionized water. In dark reactions (without irradiation), the reaction flask was protected from light with aluminum foil and keep under N_2 atmosphere. For the extraction process, CH_2Cl_2 (3 × 20 mL) was used. The organic extract was washed until no residual of DMSO remained, then dried with Na_2SO_4, filtered, and evaporated under reduced pressure.

General Procedure for the Synthesis of Substituted Dibenzofurans by Photoinduced eT Reaction in Liquid Ammonia. The following procedure is representative for all reactions in $NH_{3(l)}$ as solvent (T = −33 °C). The equipment used is a closed system, composed by a 100 mL three-necked round-bottomed pyrex-flask with a Dewar condenser, N_2 inlet and NH_3 inlet (see Figure S2, SI section 1.2). The system was dried under vacuum. Liquid ammonia (100 mL), previously dried over Na metal (see Figure S3 in SI), was distilled into the flask under nitrogen atmosphere (see Figures S4 and S5 in SI). KOBu-*tert* and then the precursor of the nucleophile (the substituted phenol for photoinduced bimolecular substitution) were added to the distilled ammonia. After 15 min, the substrate (**5a**, **5b** or **5c**) was added to the mixture (or substrates **2**, Suzuki−Miyaura products, in the case of photoinduced unimolecular substitution). The reaction mixture was irradiated for the time indicated in Table 3. In dark reactions (without irradiation), the reaction flask was protected from light with aluminum foil and kept under N_2 atmosphere. After 3 h, the mixture was quenched with an excess of NH_4NO_3. The ammonia was allowed to evaporate, and deionized water (50 mL) with diluted sulfuric acid (until pH = 5) were added to the residue and extracted twice with CH_2Cl_2 (30 mL). The organic extract was dried (Na_2SO_4) and filtered. The solvent was removed under reduced pressure and product was purified either by column chromatography or semipreparative TLC or HPLC.

Spectroscopical Information on Compounds Synthesized. Spectra are in the Supporting Information section.

*Dibenzo[b,d]furan (**1a**).*[73] Isolated as a white solid by semipreparative TLC, employing as eluent a mixture pentane/CH_2Cl_2 90:10. Yield: 89% (37 mg) in step 2, 20% (12 mg) in step 3. mp 80−83 °C. ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 8.11 (d, 2H, J = 7.8 Hz); 7.64 (d, 2H, J = 8.2 Hz); 7.52 (t, 2H, J = 7.8 Hz); 7.39 (t, 1H, J = 7.5 Hz). ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 157.0 (q, 2C, C−O); 128.3 (2C, C−H); 125.0 (q, 2C); 123.8 (2C, C−H); 121.7 (2C, C−H); 112.4 (2C, C−H).

*2-Methyldibenzo[b,d]furan (**1b**)..*[13,16,69] Isolated as a white solid by semipreparative TLC, employing as eluent a mixture pentane/CH_2Cl_2 90:10. Yield: 51% (23 mg) in step 2, 57% (36 mg) in step 3. mp 42−44 °C. ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 8.05 (d, 1H, J = 8.0 Hz); 7.88 (s, 1H); 7.60 (d, 1H, J = 8.0 Hz); 7.51−7.47 (m, 2H); 7.39−7.31 (m, 2H); 2.48 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 157.2 (q, C−O); 155.3 (q, C−O);133.3 (q); 129.3 (C−H); 128.1 (C−H); 125.0 (q); 124.9 (q); 123.7 (C−H); 121.6 (2C, C−H); 112.3 (C−H); 111.9 (C−H); 21.3 (CH_3).

*2-Methoxydibenzo[b,d]furan (**1c**)..*[13,16] Isolated as a white solid by semipreparative TLC, employing as eluent a mixture pentane/CH_2Cl_2

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90:10. Yield: 49% (24 mg) in step 2, 40% (28 mg) in step 3. mp 45−47 °C. ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 8.07 (d, 1H, J = 7.7 Hz); 7.65 (sd, 1H, J = 2.6 Hz); 7.59 (d, 1H, J = 8.8 Hz); 7.54−7.47 (m, 2H); 7.36 (t, 1H, J = 7.4 Hz); 7.10 (dd, 1H, J = 8.9 Hz, 2.6 Hz); 3.90 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 157.7 (q, C−O); 157.2 (q, C−O); 151.6 (q, C−O);128.2 (C−H); 125.5 (q); 125.4 (q); 123.5 (C−H); 121.8 (C−H); 116.3 (C−H); 112.9 (C−H); 112.4 (C−H); 104.8 (C−H); 56.3 (CH_3).

*2-Fluorodibenzo[b,d]furan (**1d**)*..[13,16] Isolated as a white solid by semipreparative TLC, employing as eluent a mixture pentane/CH_2Cl_2 90:10. Yield: 60% (27 mg) in step 2, 15% (10 mg) in step 3. mp 87−89 °C. ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 8.11 (d, 1H, J = 7.7 Hz); 7.86 (dd, 1H, J = 8.4 Hz, J = 2.7 Hz); 7.65−7.62 (m, 2H); 7.55 (td, 1H, J = 7.8 Hz, J = 1.3 Hz); 7.40 (t, 1H, J = 7.7 Hz); 7.29 (td, 1H, J = 9.0 Hz, 2.7 Hz). ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 160.0 (d, q, C−F, J_{C-F} = 236.2 Hz); 158.1 (q, C−O); 153.1 (q, C−O); 129.0 (C−H); 126.05 (d, q, J_{C-F} = 10.5 Hz); 124.7 (q); 123.9 (C−H); 122.2 (C−H); 115.4 (d, C−H, J_{C-F} = 26.0 Hz); 113.4 (d, C−H, J_{C-F} = 9.3 Hz); 112.6 (C−H); 107.7 (d, C−H, J_{C-F} = 25.4 Hz).

*2-(tert-Butyl)dibenzo[b,d]furan (**1e**)*.[70] The product was isolated and purified as a white solid by semipreparative TLC, employing as eluent a mixture pentane/CH_2Cl_2 90:10. Yield: 67% (37 mg) in step 2, 52% (41 mg) in step 3. ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 8.16 (sd, 1H, J = 1.6 Hz); 8.12 (d, 1H, J = 7.6 Hz); 7.62−7.59 (m, 2H); 7.55−7.47 (m, 2H); 7.37 (t, 1H, J = 7.5 Hz); 1.43 (s, 9H). ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 157.4 (q, C−O); 155.2 (q, C−O); 147.0 (q); 128.0 (C_{Ar}−H); 126.0 (C_{Ar}−H); 125.4 (q); 124.6 (q); 123.6 (C_{Ar}−H); 121.6 (C_{Ar}−H); 118.1 (C_{Ar}−H); 112.3 (C_{Ar}−H); 111.7 (C_{Ar}−H); 35.5 (q); 32.2 (3C, CH_3).

*2,4-Di-tert-butyldibenzo[b,d]furan (**1f**)*. The product was isolated and purified as an oil by semipreparative TLC, employing as eluent a mixture pentane/CH_2Cl_2 90:10. Yield: 50% (34 mg) in step 2, 40% (39 mg) in step 3. ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 8.09 (d, 1H, J = 7.6 Hz); 8.00 (s, 1H); 7.64 (d, 1H, J = 8.2 Hz); 7.52−7.46 (m, 2H); 7.35 (t, 1H, J = 7.4 Hz); 1.58 (s, 9H); 1.43 (s, 9H). ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 156.9 (q, C−O); 153.4 (q, C−O); 146.7 (q); 134.8 (q); 127.7 (C_{Ar}−H); 125.4 (q); 125.0 (q); 123.5 (C_{Ar}−H); 122.6 (C_{Ar}−H); 121.4 (C_{Ar}−H); 115.9 (C_{Ar}−H); 112.3 (C_{Ar}−H); 35.6 (q); 35.3 (q); 32.2 (3C, CH_3); 30.2 (3C, CH_3). HRMS (ESI-TOF) m/z $[M + H]^+$ Calcd for $C_{20}H_{25}O$: 281.1900; Found: 281.1910.

*Dibenzo[b,d]furan-2-carbonitrile (**1g**)*.[19] The product was isolated and purified as a solid by semipreparative TLC, employing as eluent a mixture pentane/CH_2Cl_2 90:10. Yield: 31% (21 mg). mp 139−141 °C. ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 8.61 (sd, 1H, J = 1.2 Hz), 8.23 (d, J = 8.0 Hz, 1H), 7.92 (dd, 1H, J = 8.4 Hz, J = 1.6 Hz), 7.85 (d, 1H, J = 8.4 Hz), 7.73 (d, 1H, J = 8.4 Hz); 7.64 (td, 1H, J = 7.2 Hz, J = 1.2 Hz); 7.50 (td, 1H, J = 8.0 Hz, J = 0.8 Hz). ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 158.8 (C−O), 157.6 (C−O), 132.1 (C−H), 129.9 (C−H), 126.8 (C−H), 126.1 (q), 124.8 (C−H), 123.5 (q), 122.5 (C−H), 119.6 (q), 111.9 (C−H), 113.0 (C−H), 107.7 (q, C≡N).

*2,7-Dimethyldibenzo[b,d]furan (**1h**)*.[28] The product was isolated and purified as a solid by semipreparative TLC, employing as eluent a mixture pentane/CH_2Cl_2 90:10. Yield: 78% (37 mg), step 2. mp 72−74 °C. ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 7.91 (d, 1H, J = 7.8 Hz), 7.81 (s, 1H), 7.46 (d, 1H, J = 8.4 Hz), 7.41 (s, 1H), 7.28 (d, 1H, J = 8.4 Hz), 7.19 (d, 1H, J = 7.9 Hz); 2.40 (s, 3H); 2.47 (s, 3H).

*2,4-Dimethyldibenzo[b,d]furan (**1i**)*. The product was isolated and purified as a colorless oil by semipreparative TLC, employing as eluent a mixture pentane/CH_2Cl_2 70:30. Yield: 47% (32 mg). ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 8.03 (d, 1H, J = 7.6 Hz); 7.69 (s, 1H); 7.61 (d, 1H, J = 8.2 Hz); 7.48 (dt, 1H, J_1= 8.3 Hz, J_2= 1.1 Hz); 7.35 (t, 1H, J = 7.3 Hz); 7.14 (s, 1H); 2.53 (s, 3H); 2.45 (s, 3H). ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 157.2 (q, C−O); 154.2 (q, C−O); 133.2 (q); 130.3 (C_{Ar}−H); 127.9 (C_{Ar}−H); 125.4 (q); 124.5 (q); 123.6 (C_{Ar}−H); 122.0 (C_{Ar}−H); 121.7 (C_{Ar}−H); 119.0 (C_{Ar}−H); 112.4 (C_{Ar}−H); 21.3 (CH_3); 15.1 (CH_3). HRMS (ESI-TOF) m/z $[M + H]^+$ Calcd for $C_{14}H_{13}O$: 197.0961; Found: 197.0972.

*2-Fluoro-7-methyldibenzo[b,d]furan (**1j**)*. The product was isolated and purified as a white solid by semipreparative TLC, employing as eluent a mixture pentane/CH_2Cl_2 75:25. mp 127−130 °C. Yield: 64% (52 mg). ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 7.97 (d, 1H, J = 7.9 Hz); 7.81 (dd, 1H, J_1= 8.4 Hz, J = 2.6 Hz); 7.60 (dd, 1H, J_1= 8.8 Hz, J = 2.0 Hz); 7.46 (s, 1H); 7.27−7.22 (m, 2H); 2.52 (s, 3H). ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 160.0 (q, C−F, J_1= 235.9 Hz); 158.6 (q, C−O); 153.1 (q, C−O); 139.7 (q, C−CH_3); 126.3 (q, J_3= 10.4 Hz); 125.2 (C_{Ar}−H); 122.2 (q); 121.7 (C_{Ar}−H); 114.7 (C_{Ar}−H, J_2= 26.0 Hz); 113.3 (C_{Ar}−H, J_3= 9.4 Hz); 112.7 (C_{Ar}−H); 107.4 (C_{Ar}−H, J_2= 25.4 Hz); 21.4 (CH_3). HRMS (ESI-TOF) m/z $[M + H]^+$ Calcd for $C_{13}H_{10}FO$: 201.0710; Found: 201.0720.

*2-(tert-Butyl)-7-methyldibenzo[b,d]furan (**1k**)*. The product was isolated and purified as a white solid by semipreparative TLC, employing as eluent a mixture pentane/CH_2Cl_2 90:10. mp 120−122 °C. Yield: 43% (34 mg). ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 8.09 (ds, 1H, J = 1.6 Hz); 7.97 (d, 1H, J = 7.9 Hz); 7.56 (dd, 1H, J = 8.8 Hz, J = 1.6 Hz); 7.49 (d, 1H, J = 8.7 Hz); 7.42 (s, 1H); 7.20 (d, 1H, J = 7.9 Hz); 2.50 (s, 3H); 1.42 (s, 9H). ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 157.8 (q, C−O); 155.2 (q, C−O); 146.8 (q); 138.4 (q); 125.4 (C_{Ar}−H); 124.8 (C_{Ar}−H); 124.7 (q); 122.8 (q); 121.2 (C_{Ar}−H); 117.8 (C_{Ar}−H); 112.5 (C_{Ar}−H); 111.5 (C_{Ar}−H); 35.4 (q, $C(CH_3)_3$); 32.2 (C−H, 3C, CH_3); 21.9 (CH_3). HRMS (ESI-TOF) m/z $[M + H]^+$ Calcd for $C_{17}H_{19}O$: 239.1430; Found: 239.1422.

*2-Methoxy-7-(trifluoromethoxy)dibenzo[b,d]furan (**1l**)*. The product was isolated and purified as a white solid by semipreparative TLC, employing as eluent a mixture pentane/CH_2Cl_2 80:20. mp 148−151 °C. Yield: 48% (54 mg). ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 8.19 (d, 1H, J = 8.5 Hz); 7.70 (ds, 1H, J = 2.6 Hz); 7.62 (s, 1H); 7.57 (d, 1H, J = 9.0 Hz); 7.35 (d, 1H, J = 7.7 Hz); 7.14 (dd, 1H, J = 9.0 Hz, J = 2.6 Hz); 3.51 (s, 3H). ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 157.6 (q, C−O); 157.4 (q, C−O); 152.5 (q, C−O); 148.9 (q, C_{Ar}-O−CF_3, ^3J = 1.9 Hz); 124.6 (q); 124.6 (q); 122.7 (C_{Ar}−H); 121.6 (q, (125.4, 122.18, 120.3, 117.7), CF_3); 117.0 (C_{Ar}−H); 116.9 (C_{Ar}−H); 113.1 (C_{Ar}−H); 106.2 (C_{Ar}−H); 105.0 (C_{Ar}−H); 56.3 (CH_3). HRMS (ESI-TOF) m/z $[M + H]^+$ Calcd for $C_{14}H_{10}F_3O_3$: 283.0577; Found: 283.0571.

*2′-Chloro-[1,1′-biphenyl]-2-ol (**2a**)*.[24] The compound was isolated from the crude by column chromatography as an oil, employing a linear gradient of eluent composed by pentane and ethyl acetate, from 100% pentane to 90%. Yield: 58% (118 mg). ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 8.28 (s, 1H, OH); 7.48 (m, 1H); 7.36−7.34 (m, 3H); 7.235 (td, 1H, ^1J = 7.4 Hz, ^2J = 1.6 Hz); 7.12 (dd, 1H, ^1J = 7.6 Hz, ^2J = 1.6 Hz); 6.97 (dd, 1H, ^1J = 8.0 Hz, ^2J = 0.8 Hz); 6.91 (td, 1H, ^1J = 7.4 Hz, ^2J = 0.8 Hz). ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 155.1 (q, C−OH); 138.6 (q, C−Cl); 134.3 (q); 132.8 (C−H); 131.6 (C−H); 129.91 (C−H); 129.88 (C−H); 129.4 (C−H); 127.3 (C−H); 127.3 (q); 120.0 (C−H); 116.4 (C−H).

*2′-Chloro-5-methyl-[1,1′-biphenyl]-2-ol (**2b**)*.[71] The compound was isolated from the crude by column chromatography as a solid, employing a linear gradient of eluent composed by pentane and ethyl acetate, from 100% pentane to 90%. Yield: 67% (37 mg). mp 163−165 °C. ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 8.04 (s, 1H, OH); 7.47 (m, 1H); 7.34−7.33 (m, 3H); 7.04 (dd, 1H, ^1J = 8.2 Hz, ^2J = 1.6 Hz); 6.93 (sd, 1H, ^2J = 1.6 Hz); 6.86 (d, 1H, ^1J = 8.0 Hz); 2.27 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 153.1 (q, C−OH); 139.05 (q, C−Cl); 134.6 (q); 132.9 (C−H); 132.1 (C−H); 130.49 (C−H); 130.1 (C−H); 129.5 (C−H); 128.9 (q); 127.5 (C−H); 127.3 (q); 116. (C−H); 20.5 (CH_3).

*2′-Chloro-5-methoxy-[1,1′-biphenyl]-2-ol (**2c**)*. The product was isolated and purified as an oil by semipreparative HPLC, employing as eluent a gradient from 50:50 to 90:10 of a mixture acetonitrile/water and a constant flow of 2 mL/min. Yield: 15% (35 mg). ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 7.83 (s, 1H, OH); 7.49−7.43 (m, 1H); 7.37−7.33 (m, 3H); 6.90 (d, 1H, ^1J = 8.2 Hz); 6.83 (dd, 1H, ^1J = 8.0 Hz, ^2J = 2.8 Hz); 6.706 (d, 1H, ^1J = 8.0 Hz); 3.75 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 153.6 (q, C−OH); 149.2 (q, C−O); 138.8 (q, C−Cl); 134.4 (q); 132.9 (C_{Ar}−H); 130.1 (C_{Ar}−H); 129.6 (C_{Ar}−H); 127.9 (q); 127.5 (C_{Ar}−H); 117.3 (C_{Ar}−H); 116.8 (C_{Ar}−H); 115.4 (C_{Ar}−H); 55.9 (CH_3). HRMS (ESI-TOF) m/z $[M + Na]^+$ Calcd for $C_{13}H_{11}ClO_2Na$: 257.0340; Found: 257.0319.

*2′-Chloro-5-fluoro-[1,1′-biphenyl]-2-ol (**2d**)*. The product was isolated and purified as an oil by semipreparative HPLC, employing as eluent a gradient from 70:30 to 90:10 of a mixture acetonitrile/

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water and a constant flow of 2 mL/min. Yield: 10% (22 mg). ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 8.27 (s, 1H, OH); 7.51−7.49 (m, 1H); 7.38−7.37 (m, 3H); 7.04−6.95 (m, 2H); 6.91 (dd, 1H, ^1J = 9.0 Hz, ^2J = 2.9 Hz). ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 156.9 (q, C−F, d, $^1J_{F-C}$= 234.0 Hz); 151.7 (q, C−OH); 137.8 (q); 134.4 (q, C−Cl); 132.9 (C_{Ar}−H); 130.3 (C_{Ar}−H); 130.0 (C_{Ar}−H); 128.7 (q, d, $^3J_{F-C}$= 7.8 Hz); 127.7 (C_{Ar}−H); 117.9 (C_{Ar}−H, d, $^2J_{F-C}$= 23.1 Hz); 117.6 (C_{Ar}−H, d, $^3J_{F-C}$= 8.1 Hz); 116.2 (C_{Ar}−H, d, $^2J_{F-C}$= 22.7 Hz). HRMS (ESI-TOF) m/z $[M - H]^-$ Calcd for $C_{12}H_7ClFO$: 221.0175; Found: 221.0171.

*5-(tert-Butyl)-2′-chloro-[1,1′-biphenyl]-2-ol (**2e**).* The compound was isolated from the crude by column chromatography as a pale yellow oil, employing a linear gradient of eluent composed by pentane and CH_2Cl_2, from a ratio 90:10 to a 50:50. Yield: 40% (52 mg). ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 8.04 (s, 1H, OH); 7.49−7.47 (m, 1H); 7.36−7.31 (m, 3H); 7.28 (dd, 1H, ^1J = 8.4 Hz, ^2J = 2.4 Hz); 7.17 (sd, 1H, ^2J = 2.4 Hz); 6.90 (d, 1H, ^1J = 8.4 Hz); 1.31 (s, 9H, 3xCH_3). ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 153.0 (q, C−OH); 142.5 (q, C−Cl); 139.3 (q); 134.6 (q); 133.2 (C−H); 130.2 (C−H); 129.4 (C−H); 128.7 (C−H); 127.4 (C−H); 126.8 (C−H); 116.2 (C−H); 116.1 (q); 34.6 (q); 31.9 (3C, CH_3). HRMS (ESI-TOF) m/z $[M - H]^-$ Calcd for $C_{16}H_{16}ClO$: 259.0884; Found: 259.0886.

*3,5-Di-tert-butyl-2′-chloro-[1,1′-biphenyl]-2-ol (**2f**).* The compound was isolated from the crude by column chromatography as a colorless oil, employing a linear gradient of eluent composed by pentane and ethyl acetate, from 100% pentane to 95%. Yield: 20% (32 mg). ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 7.52−7.49 (m, 1H); 7.38−7.37 (m, 4H); 6.7 (sd, 1H, ^2J = 2.4 Hz); 6.85 (s, 1H, OH); 1.46 (s, 9H, 3xCH_3); 1.31 (s, 9H, 3xCH_3). ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 150.9 (q, C−OH); 142.0 (q, C−Cl); 138.4 (q); 136.8 (q); 135.1 (q); 133.6 (C−H); 130.7 (C−H); 130.1 (C−H); 128.1 (C−H); 127.5 (q); 126.0 (C−H); 124.4 (C−H); 35.8 (q); 34.8 (q); 32.0 (3C, CH_3); 30.2 (3C, CH_3). HRMS (ESI-TOF) m/z $[M - H]^-$ Calcd for $C_{20}H_{24}ClO$: 315.1510; Found: 315.1504.

*2′-Chloro-4′,5-dimethyl-[1,1′-biphenyl]-2-ol (**2h**).* The compound was isolated from the crude by column chromatography as an oil, employing a linear gradient of eluent composed by pentane and ethyl acetate, from 100% pentane to 97%. Yield: 25% (29 mg). ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 7.97 (s, 1H, OH); 7.29 (s, 1H); 7.20 (d, 1H, ^1J = 8.0 Hz); 7.15 (d, 1H, J = 7.6 Hz); 7.02 (dd, 1H, ^1J = 8.4 Hz, ^2J = 2.0 Hz); 6.90 (s, 1H); 6.84 (d, 1H, J = 8.0 Hz); 2.56 (s, 3H, CH_3); 2.36 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 153.2 (q, C−OH); 139.5 (q, C−Cl); 135.9 (q); 134.2 (q); 132.7 (C−H); 132.2 (C−H); 130.5 (C−H); 130.3 (C−H); 128.8 (q); 128.2 (C−H); 127.2 (q); 116.4 (C−H); 20.8 (CH_3); 20.5 (CH_3). HRMS (ESI-TOF) m/z $[M - H]^-$ Calcd for $C_{14}H_{12}ClO$: 231.0582; Found: 231.0576.

*6-(tert-Butyl)benzofuro[2,3-b]pyridine (**7**).* The product was isolated and purified as a white solid by semipreparative TLC, employing as eluent a mixture pentane/CH_2Cl_2 95:5. mp 105−108 °C. Yield: 25% (23 mg). ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 8.62 (d, 1H, J = 4.5 Hz); 8.21 (ds, 1H, J = 1.6 Hz); 7.99 (d, 1H, J = 8.3 Hz); 7.74 (d, 1H, J = 8.8 Hz); 7.61 (d, 1H, J = 8.8 Hz); 7.51−7.47 (m, 1H); 1.45 (s, 9H). ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 156.5 (q, C−O); 150.9 (q, C−O); 147.8 (q, C_{Ar}-$C(CH_3)_3$); 146.1 (C_{Ar}−H); 145.1 (q); 128.1 (C_{Ar}−H); 123.8 (q); 122.4 (C_{Ar}−H); 119.4 (C_{Ar}−H); 117.9 (C_{Ar}−H); 112.4 (C_{Ar}−H); 35.5 (q, $C(CH_3)_3$); 32.0 (3C, CH_3). HRMS (ESI-TOF) m/z $[M + H]^+$ Calcd for $C_{15}H_{16}NO$: 226.1226; Found: 226.1218.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.8b00742.

^{1}H NMR, ^{13}C NMR and 2D NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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