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Synthesis of Dihydroisobenzofurans *via* Palladium-Catalyzed Sequential Alkynylation/Annulation of 2-Bromobenzyl and 2-Chlorobenzyl Alcohols under Microwave Irradiation

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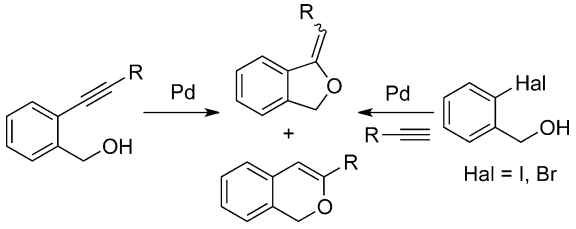
Abstract: The palladium-catalyzed synthesis of dihydroisobenzofurans has been performed by sequential Sonogashira cross-coupling/cyclization reactions between terminal alkynes and 2-(hydroxymethyl)bromo- and chlorobenzenes in methanol as solvent at 130 °C under microwave irradiation. A 4,4′-dichlorobenzophenone oxime-derived chloro-bridged palladacycle is an efficient pre-catalyst to perform this tandem process using 2-dicyclohexylphosphanyl-2′,4′,6′-triisopropylbiphenyl (Xphos) as ancillary ligand and potassium hydroxide as base in the absence of a copper cocatalyst. Under these conditions, functionalized 2-bromo- and 2-chlorobenzaldehydes are also suitable partners in the domino process affording phthalans in good yields. All the reactions can be performed under air and employing reagent-grade chemicals under low loading conditions (1 mol% Pd).

Keywords: alkynes; cycloisomerization; dihydroisobenzofurans; microwaves; palladium; Sonogashira reaction

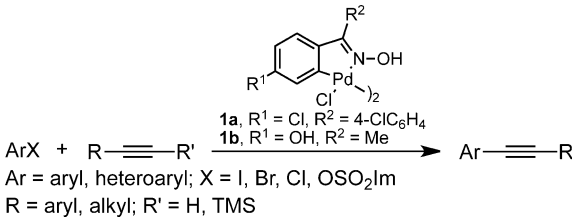
Introduction

The transition metal-catalyzed addition of nucleophiles to unactivated carbon-carbon multiple bonds[1] is of major importance in synthetic organic chemistry due to its step- and atom-economic nature.[2] Palladium[3] is the most versatile and widely used metal for this type of processes. Particularly, the intramolecular cyclization of palladium π-alkene and π-alkyne complexes bearing an internal nucleophile is a very efficient method for the synthesis of a wide variety of heterocycles,[4] compounds which have attracted extensive attention for a long time due to their remarkable biological activities. The Pd(II)-catalyzed cyclization of alkynes bearing an oxygen nucleophile has been employed for the regioselective synthesis of various oxygen-containing heterocycles such as 1,3-dihydroisobenzofurans, which are useful building blocks and key structural units in numerous natural products and drugs.[5] In general, these compounds have been prepared from the corresponding 2-(alkynyl)benzyl alcohols *via* an intramolecular hydroalkoxylation,[6] reaction which might suffer from stereo- and regioselectivity problems since both the 6-*endo-dig* and 5-*exo-dig* cyclizations are allowed by Baldwin's rules (Scheme 1). In order to gain versatility and simplicity, a tandem Sonogashira–Hagihara coupling/intramolecular hydroalkoxylation would be desirable, an approach which has been barely studied using (2-iodophenyl)methanol and (2-bromophenyl)methanol derivatives under Pd[7] or Cu[8] catalysis (Scheme 1).[9] Finally, a copper-free protocol to avoid the homocoupling of alkynes (major limitation in the conventional Sonogashira reaction involving less reactive aryl bromides and chlorides) would be attractive as well.

In recent years, we have demonstrated the high activity of oxime palladacycles as source of palladium nanoparticles[10] in a wide variety of cross-coupling reactions using organic and aqueous solvents.[11] In par-



Scheme 1. Sonogashira coupling and/or intramolecular hydroalkoxylation towards 1,3-dihydroisobenzofurans.

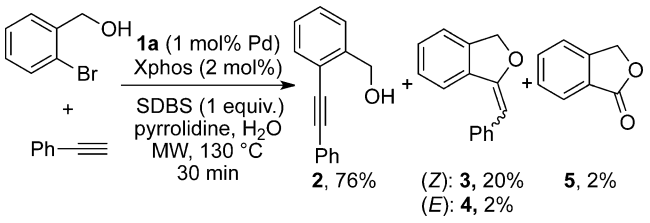


Scheme 2. Sonogashira coupling catalyzed by oxime palladacycles.[12]

ticular, palladacycles derived from 4,4′-dichlorobenzophenone oxime **1a** and 4-(hydroxy)acetophenone oxime **1b** have been shown as very active precatalysts in the copper-free Sonogashira–Hagihara coupling of aryl halides and aryl imidazolylsulfonates with terminal alkynes (Scheme 2).[12] In continuation of our exploration on the application of oxime palladacycles in C(*sp*)−C(*sp*^{2}) cross-couplings, herein we describe the stereo- and regioselective synthesis of 3-alkylidene-1,3-dihydroisobenzofurans[13] *via* Cu-free Pd-catalyzed sequential Sonogashira alkynylation/hydroalkoxylation of functionalized aryl bromides and aryl chlorides under microwave irradiation conditions.

Results and Discussion

Initially, the reaction between 2-bromobenzyl alcohol and phenylacetylene was studied under conditions similar to those previously employed in our group for the Sonogashira alkynylation of aryl bromides and chlorides using water as solvent and microwave irradiation.[12c] Thus, 2-bromobenzyl alcohol reacted with phenylacetylene in the presence of oxime palladacycle **1a** (1 mol% Pd), sodium dodecyl benzenesulfonate (SDBS, 1 equiv.) as additive, 2-dicyclohexylphosphanyl-2′,4′,6′-triisopropylbiphenyl (Xphos, 2 mol%)[14] as ancillary ligand, and pyrrolidine (2 equiv.) as base (Scheme 3). With an initial microwave irradiation of 40 W, the reaction temperature was maintained at 130 °C for 30 min. Under these conditions, the Sonogashira coupling product **2** was obtained in a 76% yield (CG and ^{1}H NMR analysis) and only a 22% yield of 1-benzylidene-1,3-dihydroisobenzofurans **3** and **4** was observed as a 91/9 *Z*/*E* mixture of diastereomers. Also, trace amounts of isobenzofuran-1(3*H*)-one (**5**) and benzaldehyde were detected in the crude reaction mixture. Then, an optimization of the reaction conditions was carried out in order to improve the yield and selectivity of the process. Selected experiments are reported in Table 1.[15]



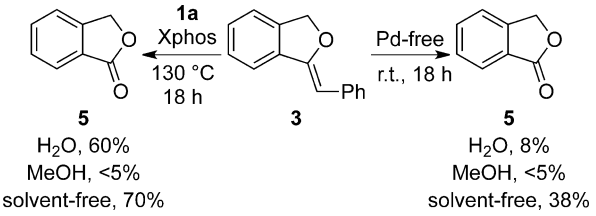
Scheme 3. Sonogashira/hydroalkoxylation of 2-bromobenzyl alcohol.

Table 1. Sonogashira/hydroalkoxylation reaction of 2-bromobenzyl alcohol with phenylacetylene in water. Reaction conditions optimization.[a]

Entry	Ligand[b]	Additive[c]	Base	Yield [%][d]	**2/3/4/5**[e]
1	Xphos	SDBS	KOH[f]	99	27/62/4/7
2	Xphos	SDBS	KOH	99	12/85/3/0
3	Xphos	SDBS	K_2CO_3	81	26/42/9/23
4	Xphos	SDBS	NaOH	99	35/40/5/20
5	Xphos	TBAB	KOH	53	2/93/2/3
6	Xphos	CTAB	KOH	50	3/95/1/1
7	Xphos	PTS	KOH	78	57/40/2/1
8	Xphos	–	KOH	84	36/61/2/1
9	–	SDBS	KOH	24	9/91/0/0
10	–[g]	SDBS	KOH	99	18/78/2/2
11	Cy_3P	SDBS	KOH	70	19/72/2/7
12	**Xphos**	**SDBS**	**KOH[h]**	**93 (65)**	**2/93/5/0**
13	Xphos	TBAB	KOH[h]	49	2/96/3/0
14	Xphos	SDBS	KOH[i]	90	27/67/3/3
15	Xphos	SDBS	KOH[j]	91	10/68/5/17

[a] *Reaction conditions:* **1a** (1 mol% Pd), ligand (2 mol%), additive (1 equiv.), base (4 equiv.), H_2O, MW, 130 °C, 30 min.
[b] Xphos = 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl; Davephos = 2-dicyclohexylphosphino-2′-(*N*,*N*-dimethylamino)biphenyl.
[c] SDBS = sodium dodecyl benzenesulfonate; TBAB = tetra-*n*-butylammonium bromide; CTAB = hexadecyltrimethylammonium bromide; PTS = polyoxyethanyl-α-tocopheryl sebacate.
[d] Conversion determined by ^{1}H NMR analysis. In parenthesis, isolated yield after silica-gel preparative chromatography.
[e] Determined by ^{1}H NMR of the crude reaction mixture.
[f] 2 equiv. of base were used.
[g] Davephos was used as ligand.
[h] Reaction time 1 h.
[i] Catalyst **1b** (1 mol% Pd) was used.
[j] The reaction was performed under conventional thermal conditions (130 °C, 15 h).

Using similar reaction conditions as those shown in Scheme 3, a base study was initially performed in order to improve the yield and selectivity of the hydroalkoxylation process. As depicted in Table 1, entries 1–4, the best result in terms of yield and selectivity was obtained using 4 equivalents of KOH as base (entry 2). Clearly, shifting from pyrrolidine to KOH as base promoted the cycloisomerization process. With respect to the surfactant, even though cationic tetra-*n*-butylammonium bromide (TBAB) and hexadecyltrimethylammonium bromide (CTAB) improved



Scheme 4. Stability studies of **3**.

the selectivity of the reaction towards **3** (Table 1, entries 5 and 6), the conversion of the process decreased significantly. On the other hand, the non-ionic surfactant polyoxyethanyl-α-tocopheryl sebacate (PTS) afforded, as a major product, the Sonogashira compound **2** (entry 7). The absence of surfactant led to a decrease in the conversion to **3** (entry 8). Regarding the ligand study, when the reaction was carried out under ligand-free conditions, a low 24% conversion was obtained in the process (Table 1, entry 9). On the other hand, as shown in entries 10 and 11, other dicyclohexylphosphine-derived ligands[15] such as tricyclohexylphosphine and 2-dicyclohexylphosphino-2′-(*N,N*-dimethylamino)biphenyl (Davephos) did not improve the result obtained with Xphos as ancillary ligand.

The reaction time for the best two experiments using water as solvent (Table 1, entries 2 and 5) was increased to 1 h, affording, in the case of SDBS the best result obtained in the study so far furnishing compound **3** in a 65% isolated yield (Table 1, entry 12). Also, the activity of catalyst **1b** under the optimized reaction conditions was tested in the model reaction. As depicted in Table 1, entry 14, **1b** afforded lower conversion towards compound **3** than palladacycle **1a**. Finally, the efficiency of the microwave irradiation in this process was demonstrated since a very low selectivity was observed when the reaction between 2-bromobenzyl alcohol and phenylacetylene was performed under conventional thermal conditions (130 °C, 15 h, Table 1, entry 15).

Next step in our study was to analyze the reasons behind the low isolated yield obtained for compound **3** under the optimized reaction conditions using water as solvent. As mentioned above, different amounts of isobenzofuran-1(3*H*)-one (**5**) and benzaldehyde were detected in many of the crude reactions (CG and ^{1}H NMR analysis). The oxidation of the benzylidene moiety[16] of the dihydroisobenzofuran by molecular oxygen would explain the formation of the observed by-products. In fact, when stirring pure compound **3** in water under aerobic conditions for 18 h, the formation of isobenzofuran-1(3*H*)-one (**5**) (8% conversion, ^{1}H NMR analysis) was observed (Scheme 4). Similarly, a 38% conversion towards **5** was detected when stirring **3** under aerobic solvent-free conditions, and a 3% conversion when stirring for 18 h in MeOH (Scheme 4). The stability experiments with **3** were

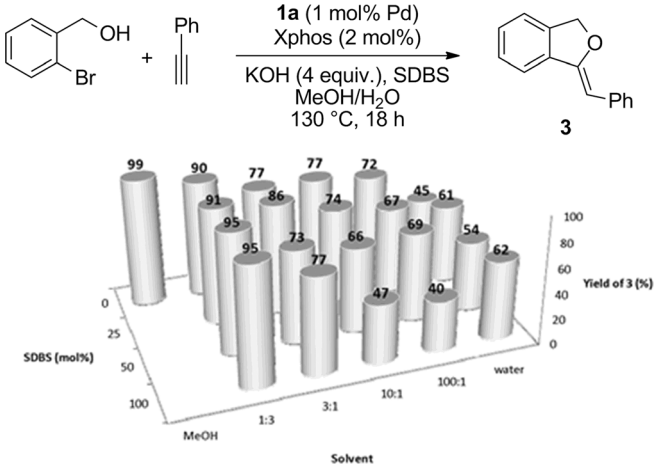


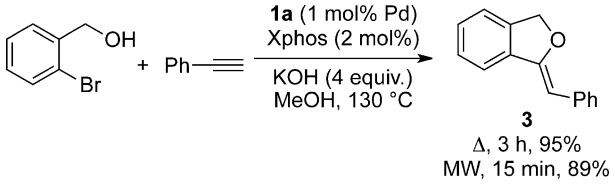
Figure 1. Sonogashira/hydroalkoxylation of 2-bromobenzyl alcohol. Solvent and surfactant study.

also carried out under the optimized reaction conditions for the Sonogashira/annulation process but in the absence of phenylacetylene. As depicted in Scheme 4, good conversions of compound **3** to isobenzofuran-1(3*H*)-one (**5**) were observed using water (60% conversion, ^{1}H NMR analysis) as solvent as well as under solvent-free conditions (70% conversion).[17,18]

At this point, we decided to perform a solvent study in order to improve the isolated yield of **3**. This solvent should also allow to use a straightforward method to isolate (*Z*)-1-benzylidene-1,3-dihydroisobenzofuran (**3**) avoiding additional decomposition processes. From the above-mentioned stability studies (Scheme 4), MeOH was chosen to perform a study where the amount of water as cosolvent and surfactant (SDBS) were varied. The study was carried out using the most challenging conventional thermal heating conditions as previously demonstrated using water as solvent (Table 1, entry 15). As depicted in Figure 1, the study showed straight MeOH in the absence of surfactant as the best conditions to carry out the Sonogashira/hydroalkoxylation reaction between 2-bromobenzyl alcohol and phenylacetylene with high yield and complete selectivity towards the formation of **3**.

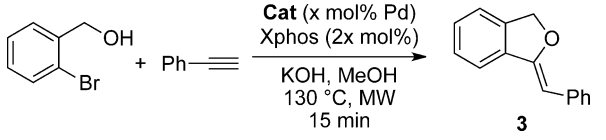
The absence of by-products when using straight MeOH as solvent allowed an easy and straightforward purification of dihydroisobenzofuran **3** from the crude reaction mixture by recrystallization. Thus, after only 3 h reaction time, pure **3** was obtained in a 95% isolated yield (Scheme 5). On the other hand, under similar reaction conditions but using microwave heating (40 W initial irradiation), (*Z*)-1-benzylidene-1,3-dihydroisobenzofuran (**3**) was obtained in an 89% isolated yield only after 15 min (Scheme 5).

Finally, a loading and catalyst study was carried out under the optimized reaction conditions using microwave heating (Table 2). The reaction did not work in



Scheme 5. Optimized conditions for the synthesis of (*Z*)-1-benzylidene-1,3-dihydroisobenzofuran (**3**) in MeOH.

Table 2. Sonogashira/hydroalkoxylation of 2-bromobenzyl alcohol with phenylacetylene in MeOH. Catalyst study.

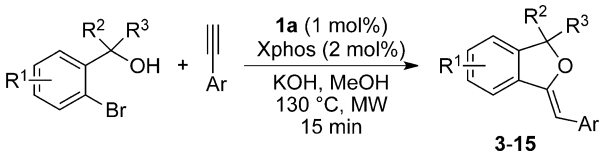


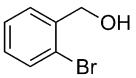
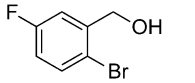
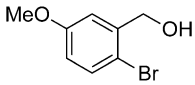
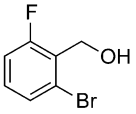
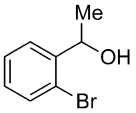
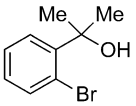
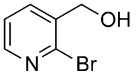
Entry	Pd Catalyst (mol% Pd)	Yield [%][a]
1	**1a** (1)	89 (0/100/0/0)
2	–	<5
3	**1a** (1)[b]	<5
4	**1a** (0.1)	82 (5/94/0/1)
5	**1a** (0.01)	<5
6	**1b** (1)	90 (0/100/0/0)
7	**1b** (0.1)	81 (3/95/1/1)
8	$PdCl_2$ (1)	71 (0/99/0/1)
9	$PdCl_2$ (0.1)	<5
10	$Pd_2(dba)_3$ (1)	76 (0/99/0/1)
11	$Pd_2(dba)_3$ (0.1)	<5
12	**1a** (1)[c,d]	84[e] (7/93/0/0)

[a] Isolated yield of **3** after purification by crystallization in MeOH. In parenthesis, selectivity **2**/**3**/**4**/**5** determined by ^{1}H NMR analysis of the crude reaction mixture.
[b] Reaction carried out in the absence of Xphos.
[c] Reaction performed under conventional thermal heating conditions (130 °C, 3 h).
[d] A drop of Hg was added after 5 min and the reaction was run for 3 h.
[e] Conversion determined by ^{1}H NMR analysis of the crude reaction after 3 h.

the absence of catalyst, or without ligand (Table 2, entries 2 and 3). In general, under the optimized conditions, all the tested Pd(II) and Pd(0) catalysts showed good isolated yields of (*Z*)-1-benzylidene-1,3-dihydroisobenzofuran (**3**) when using 1 mol% Pd as catalyst loading (Table 2, entries 1, 6, 8, and 10). However, when the catalyst loading was significantly reduced to 0.1 mol% of Pd (Table 2, entries 4, 7, 9, and 11) only palladacycle **1b** showed comparable activity to **1a** (entries 4 and 7). These latter results could be an indication of the existence of an induction period for the nanoparticles formation. However, in this particular tandem process, a mercury poisoning experiment performed on the reaction under thermal conditions (see the Supporting Information) pointed to the involvement of other different catalytically active species (Table 2, entry 12).

Table 3. Sonogashira/hydroalkoxylation of 2-bromobenzyl alcohols with terminal alkynes. Substrate study.



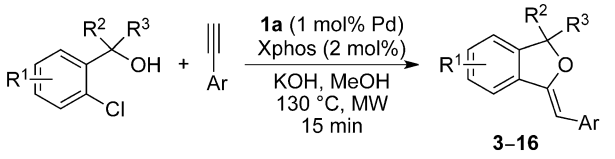
Entry	ArBr	Ar—	Product No.	Yield [%][a]
1		Ph—	**3**	89
2		4-$CF_3C_6H_4$—	**6**	75
3		4-$MeOC_6H_4$—	**7**	91
4		4-$MeOCOC_6H_4$—	**8**	94[b]
5		4-MeC_6H_4—	**9**	82
6		Ph—	**10**	73
7		Ph—	**11**	70
8		Ph—	**12**	68
9		Ph—	**13**	43
10		Ph—	**14**	46
11		Ph—	**15**	72

[a] Isolated yield after purification by crystallization in MeOH.
[b] Compound **8** was obtained as (*Z*)-4-(isobenzofuran-1(3*H*)-ylidenemethyl)benzoic acid as a consequence of the ester hydrolysis under the reaction conditions.

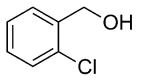
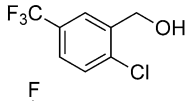
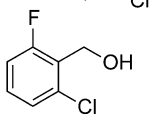
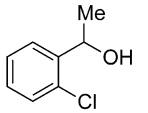
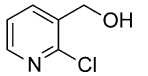
To test the effectiveness of the optimized catalytic system in the Pd-catalyzed Sonogashira coupling in MeOH, various terminal alkynes were examined in the reaction with different 2-bromobenzylic alcohols (Table 3). As previously described for phenylacetylene, 2-bromobenzyl alcohol afforded 1,3-dihydroisobenzofurans **6**–**9** with isolated yields ranging from 75 to 94% after reaction with different electron-rich and electron-poor phenylacetylene derivatives under the optimized reaction conditions (Table 3, entries 2–5).

On the other hand, functionalized 2-bromobenzylic alcohols, such as (2-bromo-5-fluorophenyl)methanol, (2-bromo-5-methoxyphenyl)methanol, and (2-bromo-6-fluorophenyl)methanol reacted with phenylacetylene to yield dihydroisobenzofurans **10**–**12** with yields of 73, 70 and 68%, respectively (entries 6–8). The sequential Sonogashira cross-coupling/cyclization process showed a certain degree of dependence with the

Table 4. Sonogashira/hydroalkoxylation of 2-chlorobenzyl alcohols with terminal alkynes in MeOH. Substrate study.



3–16

Entry	ArCl	Ar—	Product No.	Yield [%][a]
1		Ph—	**3**	81
2		4-$CF_3C_6H_4$—	**6**	48
3		4-$MeOC_6H_4$—	**7**	84
4		4-$MeOCOC_6H_4$—	**8**	80
5		4-MeC_6H_4—	**9**	75
6		Ph—	**16**	70
7		Ph—	**12**	64
8		Ph—	**13**	31
9		Ph—	**15**	73

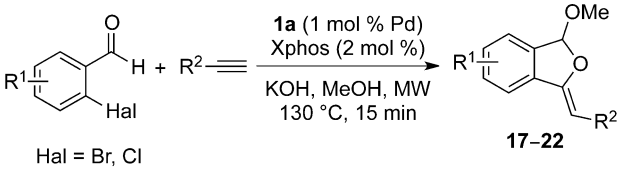
[a] Isolated yield after purification by crystallization in MeOH.

steric hinderance around the benzylic alcohol moiety since low yields were observed when secondary and tertiary alcohols where employed in the process. Thus, as depicted in entries 9 and 10, the reaction of 1-(2-bromophenyl)ethanol and 2-(2-bromophenyl)propan-2-ol with phenylacetylene, afforded compounds **13** and **14** in 43 and 46% yields, respectively. Finally, a good isolated yield was also obtained for the coupling of (2-bromopyridin-3-yl)methanol with phenylacetylene, a reaction which led to the formation of (*Z*)-7-benzylidene-5,7-dihydrofuro[3,4-b]pyridine (**15**) in a 72% isolated yield (Table 3, entry 11).

The optimized reaction conditions for the Sonogashira alkynylation/annulation process of aryl bromides were also applied to the synthesis of functionalized dihydroisobenzofurans from aryl chlorides (Table 4). In general, aryl chlorides afforded the corresponding products with similar or slightly lower yields than aryl bromides. As illustrated in Table 4 entries 1–5, (2-chlorophenyl)methanol reacted with phenylacetylene, 4′-trifluoromethylphenylacetylene, 4′-methoxyphenylacetylene, methyl 4-ethynylbenzoate, and 4′-tolylacetylene to give dihydroisobenzofurans **3**, and **6**–**9** in good isolated yields (75–85%) with the exception of the reaction with the electron-poor 4′-trifluoromethylphenylacetylene, which afforded compound **6** in a 48% yield, a result which is in accordance with the low reactivity shown by alkynes bearing electron-withdrawing groups in the Sonogashira reaction (entry 2). Functionalized aryl chlorides such as [2-chloro-5-(trifluoromethyl)phenyl]methanol and (2-chloro-6-fluorophenyl)methanol, yielded compounds **16** and **12** in 70 and 64% yields, respectively, on reaction with phenylacetylene (Table 4, entries 6 and 7). As commented above for aryl bromides, tertiary alcohols showed low reactivity in the studied process. In the same way, dihydroisobenzofuran **13** was obtained in a 31% yield by reaction of 1-(2-chlorophenyl)ethanol with phenylacetylene (entry 8). Finally, (*Z*)-7-benzylidene-5,7-dihydrofuro[3,4-b]pyridine (**15**) was isolated in a 73% yield from (2-chloropyrid-3-yl)methanol and phenylacetylene (Table 4, entry 9).

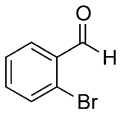
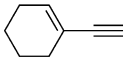
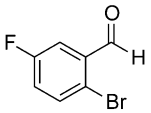
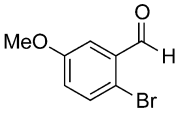
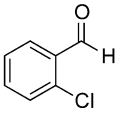
2-Alkynylbenzaldehydes have been used as versatile building blocks for the generation of a wide variety of cyclic compounds.[19] Dihydroisobenzofurans have been synthesized by a palladium-catalyzed domino addition/annulation process of *ortho*-alkynylbenzaldehydes in the presence of alcohols as nucleophiles.[6b,20,21] More recently, a variety of substituted dihydroisobenzofurans have been synthesized by a one-pot three component Pd(0)/Cu(I)-catalyzed domino reaction of *o*-bromobenzaldehydes, methanol and terminal alkynes under microwave irradiation.[22] As depicted in Table 5, oxime palladacycle **1a** in the pres-

Table 5. Sonogashira/hydroalkoxylation of 2-bromobenzyl alcohols with terminal alkynes. Substrate study.



Hal = Br, Cl

17–22

Entry	ArBr(Cl)	R^2—	Product No.	Yield [%][a]
1		Ph—	**17**	79
2		4-$CF_3C_6H_4$—	**18**	59
3		4-$MeOC_6H_4$—	**19**	62
4			**20**	52
5		Ph—	**21**	72
6		Ph—	**22**	71
7		Ph—	**17**	50

[a] Isolated yield after purification by preparative thin layer chromatography.

ence of Xphos as ligand, is an excellent catalytic system for the synthesis of 3-methoxy-1,3-dihydroisobenzofurans from 2-bromobenzaldehydes *via* multicomponent reaction with the solvent and terminal alkynes. In this way, compounds **17**–**22** were prepared in yields ranging from 52 to 79% in only 15 min under microwave irradiation (Table 5, entries 1–6). Finally, the methodology was also applied to 2-chlorobenzaldehyde which, after reaction with MeOH and phenylacetylene, afforded (*Z*)-1-benzylidene-3-methoxy-1,3-dihydroisobenzofuran (**17**) in a 50% isolated yield.

Conclusions

We have disclosed a palladium-catalyzed copper-free synthesis of dihydroisobenzofurans *via* sequential Sonogashira alkynylation/annulation of functionalized 2-bromo- and 2-chlorobenzylic alcohols as well as benzaldehydes under microwave irradiation. This reaction is carried out in the presence of Xphos as ligand (2 mol%) and the bench stable oxime palladacycle **1a** as precatalyst under low loading conditions (1 mol% Pd). The use of microwave heating and MeOH as solvent are crucial for the tandem process.

Experimental Section

General Remarks

Unless otherwise noted all commercial reagents and solvents were used without further purification. All the employed surfactants tetra-*n*-butylammonium bromide, hexadecyltrimethylammonium bromide, polyoxyethanyl-α-tocopheryl sebacate, and sodium dodecyl benzenesulfonate were commercially available and were used without further purification. All ligands and palladium catalysts were commercially available. Melting points were determined with a Reichert Thermovar hot plate apparatus and were not corrected. IR spectra were recorded on a Nicolet 510 P-FT apparatus. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were obtained on a Bruker AC-300, using $CDCl_3$ as solvent and TMS as internal standard, unless otherwise stated. Proton and carbon chemical shifts are given in ppm and coupling constants in Hz. Low-resolution electron impact (EI) mass spectra were obtained at 70 EV on an Agilent 5973 Network Mass selective detector. High-resolution mass spectra were obtained either with an electron impact (EI, 70 eV) Agilent 7200 QTOF apparatus or with a Waters LCT Premier XE apparatus (ESI, TOF). Analytical TLC was performed on Merck aluminium sheets with silica gel 60 F254. Silica gel 60, (0.04–0.06 mm) was employed for flash chromatography. Silica gel 60 F254 containing gypsum was employed for preparative layer chromatography. Microwave reactions were performed with a CEM Discover Synthesis Unit (CEM Corp., Matthews, NC) with a continuous focused microwave power delivery system in glass vessels (10 mL) sealed with a septum under magnetic stirring. The temperature of the reaction mixture inside the vessel was monitored using a calibrated infrared temperature control under the reaction vessel.

Typical Procedure for the Sonogashira Coupling under MW Irradiation Conditions

A 10-mL MW vessel was charged with 2-bromobenzyl alcohol (0.056 g, 0.3 mmol, 1 equiv.), phenylacetylene (0.040 mL, 0.36 mmol, 1.2 equiv.), KOH (0.067 g, 1.2 mmol, 4 equiv.), catalyst 1a (0.0012 g, 1 mol% Pd), Xphos (0.0029 g, 2 mol%) and MeOH (1 mL). The vessel was sealed with a pressure lock, and the mixture was heated in air at 130 °C for 15 min with the aid of an initial 40 W MW irradiation in a CEM Discover MW reactor. After this time, the reaction mixture was extracted with EtOAc (3 × 10 mL), and the organic layers were washed with H_2O (3 × 10 mL), dried over $MgSO_4$, filtered over Celite, and concentrated under reduced pressure. The crude residue was purified by simple crystallization with cold MeOH to give the corresponding dihydroisobenzofuran **3** as a yellow solid; yield: 89%; mp 92–94 °C (MeOH); IR: ν = 3049, 1650, 1466, 1293, 1036, 814, 758, 691 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.76–7.72 (2H, m), 7.60–7.55 (1H, m), 7.39–7.30 (5H, m), 7.17–7.11 (1H, m), 5.95 (1H, s), 5.52 (2H, s); ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 156.3, 139.3, 136.4, 134.8, 128.7, 128.4, 128.1, 127.7, 125.3, 121.2, 120.0, 96.2, 74.9; MS: *m*/*z* = 209 (M^+ + 1, 18), 208 (M^+, 100), 207 (36), 193 (13), 179 (43), 178 (51), 165 (21), 89 (14).

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