Synthesis of 1-(Alkoxycarbonyl)methylene-1,3-dihydroisobenzofurans and 4-(Alkoxycarbonyl)benzo[*c*]pyrans by Palladium-Catalysed Oxidative Carbonylation of 2-Alkynylbenzyl Alcohols, 2-Alkynylbenzaldehydes and 2-Alkynylphenyl Ketones

Alessia Bacchi,[a] Mirco Costa,*[b] Nicola Della Cà,[b] Marcella Fabbricatore,[c] Alessia Fazio,[c] Bartolo Gabriele,*[d] Cristina Nasi,[b] and Giuseppe Salerno[c]

Keywords: Carbonylation / Cyclisation / Heterocycles / Palladium

A direct synthesis of 1-(alkoxycarbonyl)methylene-1,3-dihydroisobenzofurans **2** and **5** and 4-(alkoxycarbonyl)benzo[*c*]-pyrans **3** and **6** by oxidative Pd-catalysed cyclization/alkoxycarbonylation of 2-alkynylbenzyl alcohols **1**, and of 2-alkynylbenzaldehydes or 2-alkynylphenyl ketones **4** is reported. Reactions were carried out in ROH or CH_3CN/ROH (R = Me, *i*Pr) as the solvent at 70–105 °C in the presence of catalytic amounts of PdI_2 in conjunction with KI under a 4:1 or 3:1 CO/air mixture (2.0 or 3.2 MPa total pressure at 25 °C). The reaction occurs through intramolecular attack by the nucleophilic oxygen atom (either already present in the starting material, as in **1**, or generated in situ by ROH attack on carbonyl group, as in **4**) on the triple bond coordinated to Pd^{II}, followed by alkoxycarbonylation. The presence of substituents at the alkyne terminal position and at the carbon atom α to the hydroxy group play a key role in the selectivity of the process towards the formation of a five- or six-membered ring.

Introduction

The use of the catalytic system based on PdI_2 in conjunction with an excess of KI in the oxidative carbonylation of alk-1-ynes, disclosed by us some years ago,[1] has proved very valuable for performing carbonylative cyclisation reactions leading to the selective formation of important heterocyclic derivatives.[2] In particular, we have recently shown that (*Z*)-2-en-4-yn-1-ols can be efficiently and selectively converted into furan-2-ylacetic esters through an *anti*-5-*exo*-*dig* cyclisation process followed by alkoxycarbonylation and aromatisation.[2] We now wish to report a new synthesis of 1-(alkoxycarbonyl)methylene-1,3-dihydroisobenzofurans **2** and **5**, and of 4-(alkoxycarbonyl)benzo[*c*]pyrans **3** and **6**, by PdI_2/KI-catalysed oxidative cyclization/alkoxycarbonylation of readily available 2-alkynylbenzyl alcohols **1** and 2-alkynylbenzaldehydes or 2-alkynylphenyl ketones **4**, according to Equations (1) and (2). Alternative cyclisation methods of low catalytic efficiency for some members of these classes of compounds have been reported to be useful in combinatorial chemistry.[3]

[a] Dipartimento di Chimica Generale ed Inorganica, Chimica Analitica, Chimica Fisica, Università di Parma,
Parco Area delle Scienze 17A, 43100 Parma, Italy
[b] Dipartimento di Chimica Organica e Industriale, Università di Parma,
Parco Area delle Scienze 17A, 43100 Parma, Italy
Fax: (internat.) + 39-0521/905-472
E-mail: mirco.costa@unipr.it
[c] Dipartimento di Chimica Università della Calabria,
87036 Arcavacata di Rende, Cosenza, Italy
[d] Dipartimento di Scienze Farmaceutiche, Università della Calabria,
87036 Arcavacata di Rende, Cosenza, Italy
Fax: (internat.) + 39-0984/492-044
E-mail: b.gabriele@unical.it
Supporting information for this article is available on the WWW under http://www.eurjoc.org or from the author.

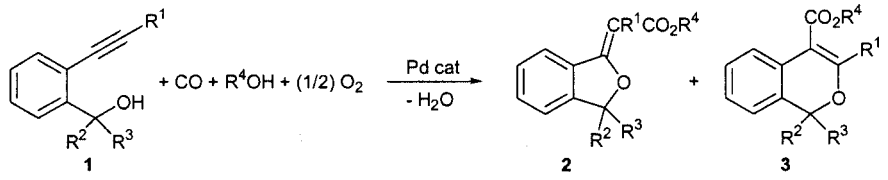
Results and Discussion

Oxidative Carbonylation of 2-Alkynylbenzyl Alcohols 1

We began our study on oxidative carbonylation of 2-alkynylbenzyl alcohols **1** with the simplest derivative, 2-ethynylbenzyl alcohol (**1a**; $R^1 = R^2 = R^3 = H$). The reaction of **1a** [carried out under the following conditions: molar ratio PdI_2/KI/**1a** = 1:10:1000, solvent MeOH, T = 70 °C, p(CO) = 1.6 MPa, p(air) = 0.4 MPa, substrate conc. = 0.22 mmol/mL MeOH] led to the formation of a mixture of three carbonylation products all containing a five-membered ethereal ring, according to Equation (3).

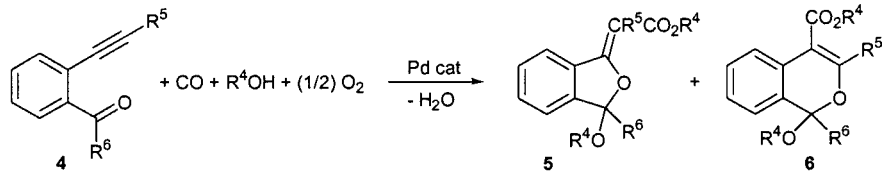
The attribution of the double bond configuration to stereoisomers (*E*)-**2a** and (*Z*)-**2a** was based on 1D and 2D ^1H NMR spectroscopic data. It is in fact very well known for similar molecules that the absorption of 7-H is strongly shifted to low field when the CO_2R group is on the same

  DOI: 10.1002/ejoc.200300577



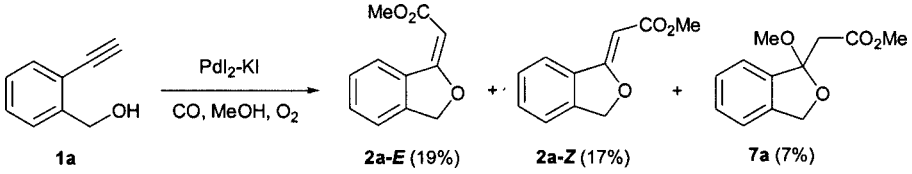
(1)

1a	$R^1 = R^2 = R^3 = H$	**2a**	$R^1 = R^2 = R^3 = H$, $R^4 = Me$
1a'	$R^1 = SiMe_3$, $R^2 = R^3 = H$	**2a**	$R^1 = R^2 = R^3 = H$, $R^4 = Me$
1b	$R^1 = Bu$, $R^2 = R^3 = H$	**2b, 3b**	$R^1 = Bu$, $R^2 = R^3 = H$, $R^4 = Me$
1c	$R^1 = Ph$, $R^2 = R^3 = H$	**2c, 3c**	$R^1 = Ph$, $R^2 = R^3 = H$, $R^4 = Me$
1d	$R^1 = R^2 = Bu$, $R^3 = H$	**2d, 3d**	$R^1 = R^2 = Bu$, $R^3 = H$, $R^4 = Me$
1e	$R^1 = Ph$, $R^2 = Bu$, $R^3 = H$	**2e, 3e**	$R^1 = Ph$, $R^2 = Bu$, $R^3 = H$, $R^4 = Me$
1f	$R^1 = Bu$, $R^2 = R^3 = Et$	**2f**	$R^1 = Bu$, $R^2 = R^3 = Et$, $R^4 = Me$
1g	$R^1 = Ph$, $R^2 = R^3 = Et$	**2g**	$R^1 = Ph$, $R^2 = R^3 = Et$, $R^4 = Me$



(2)

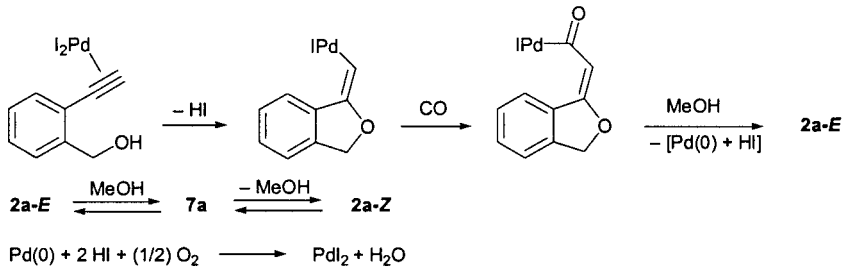
4a	$R^5 = H$, $R^6 = Me$	**5a**	$R^4 = Me$, $R^5 = H$, $R^6 = Me$	**5a'**	$R^4 = iPr$, $R^5 = H$, $R^6 = Me$
4b	$R^5 = R^6 = H$	**5b, 6b**	$R^4 = Me$, $R^5 = R^6 = H$		
4c	$R^5 = Ph$, $R^6 = Me$	**5c**	$R^4 = Me$, $R^5 = Ph$, $R^6 = Me$		
4d	$R^5 = Ph$, $R^6 = H$	**5d, 6d**	$R^4 = Me$, $R^5 = Ph$, $R^6 = H$		
4e	$R^5 = Bu$, $R^6 = Me$	**5e**	$R^4 = Me$, $R^5 = Bu$, $R^6 = Me$		
4f	$R^5 = Bu$, $R^6 = H$	**6f**	$R^4 = Me$, $R^5 = Bu$, $R^6 = H$		
4g	$R^5 = SiMe_3$, $R^6 = Me$	**5g**	$R^4 = Me$, $R^5 = SiMe_3$, $R^6 = Me$		
4h	$R^5 = SiMe_3$, $R^6 = H$	**5h, 6h**	$R^4 = Me$, $R^5 = SiMe_3$, $R^6 = H$		
4i	$R^5 = H$, $R^6 = Ph$	**5i**	$R^4 = Me$, $R^5 = H$, $R^6 = Ph$		



(3)

side of 7-H [isomer (*E*)].[4] This assignment was confirmed by ^1H-^1H NOESY experiments, which showed a strong interaction between the olefinic proton and 7-H in the case of (*Z*)-**2a** and only a weak interaction in the case of (*E*)-**2a**. The formation of isobenzofuran (**2a**) with (*E*) stereochemistry corresponds to an *anti*-5-*exo*-*dig* intramolecular nucleophilic attack by the OH group on the triple bond coordinated to Pd^{II}, followed by alkoxycarbonylation (Scheme 1; anionic iodide ligands are omitted for clarity). As shown by low-conversion experiments, products (*Z*)-**2a** derive from double-bond isomerisation of initially formed (*E*)-**2a** through MeOH addition to the vinyl ethereal bond to give **7a**, followed by MeOH elimination. The final equilibrium distribution after 2 h corresponded to 19% of (*E*)-**2a**, 17% of (*Z*)-**2a**, and 7% of **7a** (GLC yields based on starting **1a**; substrate conversion was 78%, by GLC; Run 1, Table 1).

Substrate conversion decreased when working in more dilute solutions (0.05 mmol of **1a** per mL of MeOH, Run 2) decreasing the reaction temperature (60 °C, Run 3) or increasing the KI/PdI_2 molar ratio (50:1, Run 4) gave no significant improvement in the selectivity of the process. However, a more selective reaction towards the formation of (*E*)-**2a** could be obtained by using higher CO and air pressures (3.2 and 0.8 MPa, respectively, Run 5). The reaction carried out under these conditions for 7 h (to achieve quantitative substrate conversion) afforded a fair yield of (*E*)-**2a** (52% GLC, 46% isolated) together with small amounts of (*Z*)-**2a** (10%) and **7a** (13%; Run 6).



Scheme 1

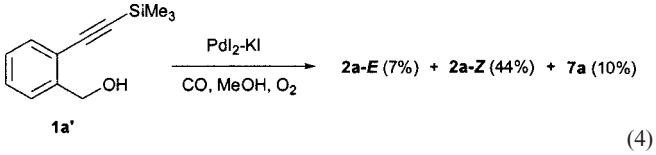
Table 1. Reactions of 2-ethynylbenzyl alcohol (**1a**) with CO/air (4:1) and MeOH in the presence of PdI_2/KI, t = 2 h, molar ratio **1a**/PdI_2 = 1000:1

Run	KI/PdI_2	T [°C]	p_{CO} [MPa]	p_{air} [MPa]	Conc. of **1a** [mol L^{-1}]	Conv. of **1a** [%][a]	Yield of (*E*)-**2a** [%][b]	Yield of (*Z*)-**2a** [%][b]	Yield of **7a** [%][b]
1	10	70	1.6	0.4	0.22	68	19	17	7
2	10	70	1.6	0.4	0.05	13	6		2
3	10	60	1.6	0.4	0.22	48	18	2	5
4	50	70	1.6	0.4	0.22	24	10		1
5	10	70	3.2	0.8	0.22	52	32	7	7
6[c]	10	70	3.2	0.8	0.22	95	52 (46)	10 (8)	13 (11)

[a] Based on starting **1a**, by GLC. [b] GLC yield (isolated yield) based on **1a**. [c] Reaction time: 7 h.

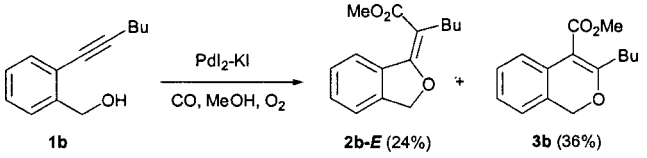
The reaction under these optimised conditions was then extended to substituted acetylenic substrates. As expected in view of their lower coordinating ability to Pd^{II}, 2-alkynylbenzyl alcohols with an internal triple bond are less reactive than **1a**, so carbonylations were carried out at higher temperatures (80−100 °C) and with a lower molar ratio of substrate/PdI_2 (with a molar ratio of substrate/catalyst of 500 or 100 rather than 1000) in order to achieve acceptable reaction rates. Moreover, with these substrates the results obtained by using 1.6 MPa of CO and 0.4 MPa of air were consistently similar to those obtained with 3.2 MPa of CO and 0.8 MPa of air.

Carbonylation of {2-[2-(trimethylsilyl)ethynyl]phenyl}-methanol (**1a′**) (R^1 = $SiMe_3$, R^2 = R^3 = H) carried out in MeOH at 80 °C for 15 h [PdI_2/KI/**1a′** = 1:10:500, p(CO) = 1.6 MPa, p(air) = 0.4 MPa, **1a′** conc. = 0.22 mmol/mL MeOH] afforded the same products (*E*)-**2a**, (*Z*)-**2a**, and **7a** already isolated from the reaction of **1a** [Equation (4)]. Starting from **1a′** under the above conditions, however, the product distribution was different with respect to that previously obtained starting from **1a** (Run 6). In fact, (*Z*)-**2a** was now the main product (50% GLC yield, 44% isolated), with (*E*)-**2a** and **7a** being formed in 11% GLC yield (7% isolated) and 14% GLC yield (10% isolated), respectively. This means that the TMS group is lost in the course of the oxidative carbonylation process.



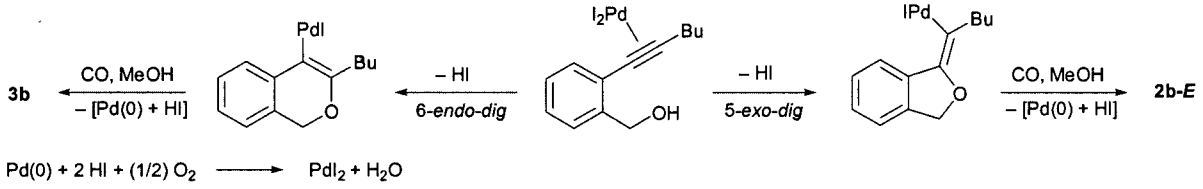
(4)

Under the same conditions employed for **1a′** (with a molar ratio of substrate/catalyst = 100:1), substrates bearing an alkyl group on the triple bond, such as [2-(hex-1-yn-1-yl)phenyl]methanol (**1b**; R^1 = Bu), afforded a mixture of benzo[*c*]pyran and dihydroisobenzofuran derivatives, the first one being the main reaction product [42% GLC yield (36% isolated) for **3b**, 25% GLC yield (24% isolated) for (*E*)-**2b** after 8 h, starting from **1b**; Equation (5)]. Therefore, in the presence of a substituent on the triple bond, the 6-*endo-dig* cyclisation mode, not observed with R^1 = H or TMS, becomes favoured (Scheme 2). This is clearly connected to the distortion exerted by the substituent on the triple-bond π*-orbital, which now assumes a geometry more favourable for an *endo* rather than an *exo* attack.[5]

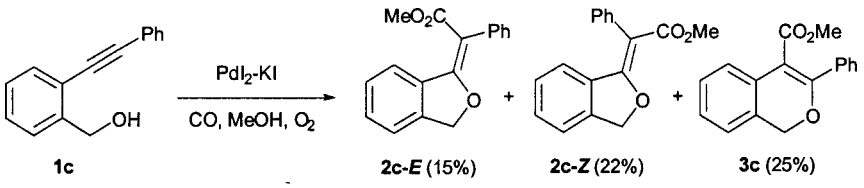


(5)

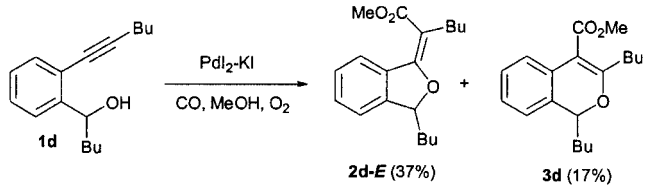
Interestingly, it was found that the nature of the substituent at the alkyne terminal position exerts a significant influence on the ratio between the five- and six-membered-ring products. Thus, substitution of a phenyl rather than an alkyl group (R^1 = Ph) at the triple bond, as in [2-(2-phenylethynyl)phenyl]methanol (**1c**), tends to slightly favour the 5-*exo-dig* cyclisation mode rather than the *6-endo-dig* cyclisation mode. This means that an electron-withdrawing group on the triple bond favours the formation of five-membered cyclic ethers. Moreover, **1c** turned out to be less reactive



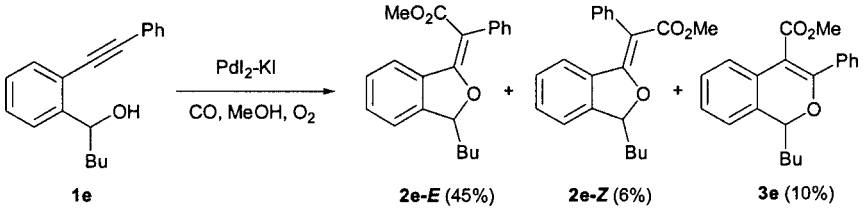
Scheme 2



(6)



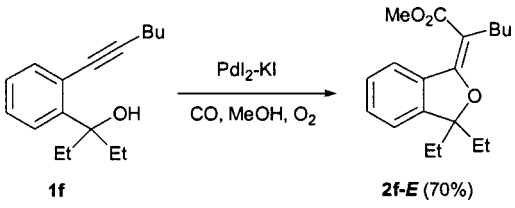
(7)



(8)

than **1b**, probably owing to the stabilisation of the triple bond ensuing from additional conjugation, so the reaction was carried out at 100 °C rather than at 80 °C. After 7 h, conversion of the substrate was practically quantitative, with formation of dihydroisobenzofurans (*E*)-**2c** and (*Z*)-**2c** [40% overall GLC yield, 15% isolated yield of (*E*)-**2c**, 22% isolated yield of (*Z*)-**2c**] and benzo[*c*]pyran **3c** [30% GLC yield, 25% isolated; Equation (6)]. An X-ray diffraction analysis confirmed the structure of **3c** (Figure S1 in the Supporting Information). Additional substitution α to the hydroxy group invariably resulted in a higher substrate reactivity and a higher tendency towards 5-*exo-dig* cyclization. Both these effects are connected to the fact that the presence of substituent(s) α to the hydroxy group tends to favour a conformation in which the OH group is closer to the triple bond (reactive rotamer effect).[6] Thus, the reaction of 1-[2-(hex-1-ynyl)phenyl]pentan-1-ol (**1d**; $R^1 = R^2 = Bu$) under the same conditions employed for **1b** was completed after 2 h with formation of dihydroisobenzofuran (*E*)-**2d** as the main product (42% GLC yield, 37% isolated) and benzo[*c*]pyran **3d** as co-product [21% GLC yield, 17% isolated; Equation (7)]. As expected, 1-[2-(2-phenylethynyl)-phenyl]pentan-1-ol (**1e**; $R^1 = Ph$, $R^2 = Bu$) is less reactive than **1d**, but rather more reactive than **1c** bearing a primary alcoholic group. The reaction of **1e** at 80 °C for 7 h led to 56% overall GLC of (*E*)-**2e** + (*Z*)-**2e** (45% isolated yield for (*E*)-**2e**, 6% for (*Z*)-**2e**) and 13% GLC yield (10% isolated) of **3e** [(Equation (8)]

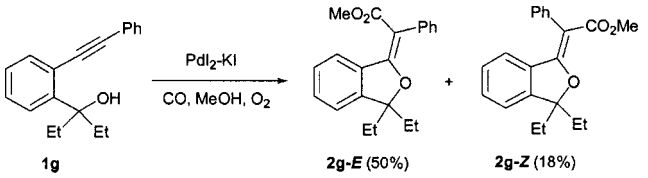
The reactive rotamer effect is particularly important in the presence of geminal dialkyl substitution α to the hydroxy group, as in 3-[2-(hex-1-ynyl)phenyl]pentan-3-ol (**1f**, $R^1 = Bu$, $R^2 = R^3 = Et$). This substrate is particularly reactive, so carbonylation could be carried out at 80 °C for 2 h with a molar ratio of **1f**/PdI_2 as high as 1000:1, with exclusive formation of the dihydroisobenzofuran derivative (*E*)-**2f** in 78% GLC yield [70% isolated, Equation (9)].



(9)

Under similar conditions, the reaction of 3-[2-(2-phenylethynyl)phenyl]pentan-3-ol (**1g**, $R^1 = Ph$, $R^2 = R^3 = Et$) led to 1,1-diethyl-3-[(methoxycarbonyl)(phenyl)methylene]-

1,3-dihydroisobenzofuran (**2g**) as a (*E*)/(*Z*) = 73:27 mixture [68% total isolated yield, Equation (10)].



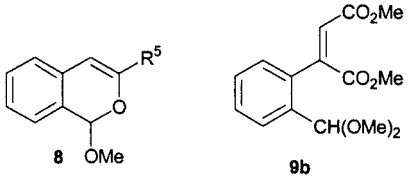
(10)

These results clearly indicate that substituents α to the hydroxy group favour the formation of the five-membered cyclic ethers, independently of the substituent at the terminal position of the alkyne.

Oxidative Carbonylation of 2-Alkynylbenzaldehydes and 2-Alkynylphenyl Ketones 4

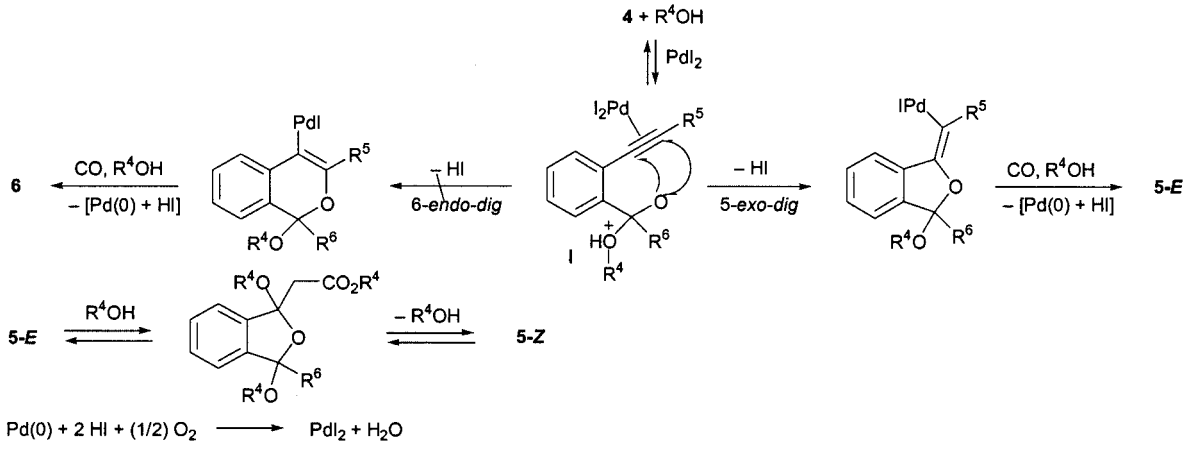
The oxygen atom of carbonyl groups of aldehydes or ketones is not nucleophilic enough to attack coordinated triple bonds. However, in the presence of nucleophiles, such as alcohols, formation of a tetrahedral intermediate ensuing from PdI_2-assisted nucleophilic attack on the carbon atom can take place and, as a consequence, the oxygen atom becomes nucleophilic and may attack activated triple bonds. Thus, oxidative carbonylation of 2-alkynylbenzaldehydes and 2-alkynylphenyl ketones **4**, carried out in the presence of MeOH or *i*PrOH under conditions similar to those employed for 2-alkynylbenzyl alcohols **1**, led to 3-alkoxy-1,3-dihydroisobenzofuran and 1-alkoxybenzo[*c*]pyran derivatives **5** and **6**, respectively [Equation (2)], through the sequence of reaction steps shown in Scheme 3, involving: (a) reversible nucleophilic attack on the carbonyl group by ROH, possibly favoured by carbonyl coordination to Pd^{II},[7] with formation of tetrahedral intermediate **I**; (b) 5-*exo-dig* or 6-*endo-dig* intramolecular nucleophilic attack by the oxygen atom on the triple bond coordinated to Pd^{II}; and (c) alkoxycarbonylation of the resulting vinylpalladium intermediates.[8a,8b] Analogously to **2**, MeOH addition/elimination to the exocyclic double bond accounts for (*E*)-**5** → (*Z*)-**5** isomerization.

Substrates **4** are significantly less reactive than 2-alkynylbenzyl alcohols **1**, because, as shown in Scheme 3, the reactive species **I** undergoing the cyclization/carbonylation process is now generated in situ in a pre-equilibrium step. Carbonylations were thus carried out at 70−105 °C for 24−48 h with a molar ratio of substrate/catalyst = 30:1 (Table 2). In some cases, compounds **8** (corresponding to cyclisation of **I** followed by protonolysis[7] rather than carbonylation, Runs 13, 14, 17, 18, 20 and 21) and maleic derivative **9b** (corresponding to oxidative dialkoxycarbonylation of the triple bond[1] and acetalization of the formyl group, Run 10) were also isolated from the reaction mixtures. We found that in several cases by-product formation could be curtailed by working in MeCN as the solvent in the presence of ROH rather than in pure ROH (compare, for example, Runs 9 and 20 with Runs 10 and 21, respectively). In particular, substrates **4a** and **4g** in MeOH as the solvent led to complex mixtures of products, which were not isolated.



d R^5=Ph
f R^5=Bu,
h R^5=TMS

As expected, substrates with a terminal triple bond (R^5 = H) are more reactive than those bearing an internal triple bond (R^5 = alkyl, aryl; compare Runs 7−10 and 22 with Runs 11−21). Substrates **4g** and **4h**, with the triple bond substituted with a TMS group, are less reactive than the corresponding substrates **4c**−**f** with the triple bond substituted with an alkyl or an aryl group (compare Runs 19−21 with Runs 11−18). Aldehydes are generally more reactive than ketones. This is likely to be due to the fact that the pre-equilibrium leading to **I** is more favourable in the case of aldehydes, so the reactive rotamer effect in this case can play a minor role in determining substrate reactivity. However, the reactive rotamer effect does affect the regioselectiv-



Scheme 3

Table 2. Reactions of 2-alkynylbenzaldehydes and 2-alkynylphenyl ketones **4** (2 mmol) with CO/air (3:1) and R^4OH in CH_3CN, initial pressure = 3.2 MPa at 25 °C, molar ratio of PdI_2/KI/**4** = 1:10:30, substrate conc. = 0.34−0.38 mol L^{-1} (in CH_3CN and R^4OH)

Run	**4**	R^5	R^6	MeCN [mL]	R^4OH [mL]	*T* [°C]	*t* [h]	Conv. of **4** [%][a]	(*E*)-**5** [%][b]	(*Z*)-**5** [%][b]	6 [%][b]	8 [%][b]	9 [%][b]
7	4a	H	Me	5	0.4[c]	80	48	99	60 (50)	22 (16)			
8	4a	H	Me	5	0.8[d]	80	48	99	32 (28)	36 (29)			
9	4b	H	H	5	0.2[c]	70	24	99	24 (18)	35 (28)	13 (9)		
10	4b	H	H	−	5.2[c]	70	24	99					66 (58)
11	4c	Ph	Me	5	0.4[c]	85	48	78	26 (19)	13			
12	4c	Ph	Me	−	5.4[c]	85	48	98	19	51 (43)			
13	4d	Ph	H	5	0.2[c]	85	24	82	4 (2)		47 (40)	16 (9)	
14	4d	Ph	H	−	5.2[c]	85	24	94	Traces		58	18	
15	4e	Bu	Me	5	0.8[c]	80	48	81	46 (39)				
16	4e	Bu	Me	−	5.8[c]	85	24	89	44				
17	4f	Bu	H	5	0.4[c]	80	48	89			55 (48)	8 (5)	
18	4f	Bu	H	−	5.4[c]	85	48	97			60	10	
19	4g	TMS	Me	5	0.4[c]	85	48	76		62 (53)			
20	4h	TMS	H	5	0.4[c]	105	48	32	15 (11)		3	10	
21	4h	TMS	H	−	5.4[c]	105	48	96			6 (4)	44 (36)	
22	4i	H	Ph	5	0.4[c]	80	48	97	28 (23)	45 (38)			

[a] Based on starting compound **4**, by GLC. [b] GLC yield (isolated yield) based on **4**. [c] R^4 = Me. [d] R^4 = *i*Pr.

ity of the process: in fact, analogously to what was observed in the case of carbonylation of benzyl alcohols **1** (see above), additional substitution α to the hydroxy group in intermediates **I** (R^6 = alkyl, aryl) tends to favour the 5-*exo*-*dig* cyclisation mechanism over the 6-*endo*-*dig* mechanism. Accordingly, isobenzofurans (*E*)-**5** and (*Z*)-**5** were obtained exclusively with ketonic substrates **4a** (R^5 = H, R^6 = Me), **4c** (R^5 = Ph, R^6 = Me), **4e** (R^5 = Bu, R^6 = Me), **4g** (R^5 = TMS, R^6 = Me) and **4i** (R^5 = H, R^6 = Ph) (Runs 7, 8, 11, 12, 15, 16, 19 and 22) and as main products with aldehyde **4b** (R^5 = R^6 = H). Formation of benzo[*c*]pyrans **6** was observed only starting from aldehydes, high selectivities being obtained in particular with substrates **4d** (R^5 = Ph, R^6 = H), **4f** (R^5 = Bu, R^6 = H) and **4h** (R^5 = TMS, R^6 = H) (Runs 13, 14, 17, 18 and 21).

Analogously to products (*E*)-**2** and (*Z*)-**2**, the attribution of the geometry around the double bond of the two isomers (*E*)-**5** and (*Z*)-**5** was based on the chemical shift of 7-H and on ^1H-^1H NOESY experiments, which, in the particular case of R^5 = H, show a clear dipolar interaction between the olefinic proton and 7-H only in the case of the (*Z*) isomer. The X-ray crystal structures of (*Z*)-**5c** and (*Z*)-**5g** allowed the univocal determination of the configuration of the substituents at the exocyclic double bond (Figures S2 and S3 in the Supporting Information). According to the mechanism shown in Scheme 3, the (*E*) isomer predominats in the MeCN/MeOH mixture (Run 11) [molar ratio of (*Z*)-**5c**/(*E*)-**5c** = 13:26] while the (*Z*) isomer is favoured in pure MeOH (Run 12) [(*Z*)-**5c**/(*E*)-**5c** = 51:19].

Conclusions

In conclusion, five-membered-ring compounds (1,3-dihydroisobenzofurans) containing an (alkoxycarbonyl)methylene chain and six-membered-ring compounds {4-(alkoxycarbonyl)benzo[*c*]pyrans} have been easily obtained through ordered Pd-catalysed reaction sequences starting from 2-alkynylbenzyl alcohols, or from the in situ formed acetals of 2-alkynylbenzaldehydes or ketals of 2-alkynyl ketones. It has been shown that the presence of substituents in the position α to the alcoholic or ketonic hydroxy group leads to the selective formation of five-membered ethereal rings. By contrast, six-membered rings are preferentially formed in the absence of at least one of these substituents as in the case of aldehyde acetals. This catalytic methodology allows the conversion, under mild conditions, of readily accessible substrates into products that may find application in pharmaceutical and biological fields.[9][10a][10b]

Experimental Section

General: Melting points were determined with a Reichert Thermovar melting point apparatus and are uncorrected. Elemental analyses were carried out with a Carlo Erba Elemental Analyzer Mod. 1106. ^1H and ^{13}C NMR spectra were taken with a Bruker AC300 spectrometer with Me_4Si as internal standard and recorded at 300 MHz and 75 MHz, respectively. Chemical shifts (δ) and coupling constants (*J*) are given in ppm and Hz, respectively. IR spectra were taken with a Perkin−Elmer Paragon 1000 PC FT-IR spectrometer. Mass spectra were obtained using an HP 5972A GC-MS apparatus at 70 eV ionisation voltage. All reactions were analysed by TLC on silica gel 60 F_{254} or by GLC using a Shimadzu GC-14A or a gas chromatograph and capillary columns with polymethylsilicone + 5% phenylsilicone as the stationary phase (HP-5). Column chromatography was performed on silica gel 60 (Merck, 70−230 mesh).

Preparation of Substrates: The 2-alkynylbenzyl alcohols **1a**−**g** and **1a′** were prepared as already described.[11] Substrates **4a**−**i** were prepared according to the procedures reported in the literature.[12a−12g]

Typical Procedure for Oxidative Carbonylation of 2-Alkynylbenzyl Alcohols 1 to 1-(Alkoxycarbonyl)methylene-1,3-dihydroisobenzofurans 2 and 4-(Alkoxycarbonyl)benzo[*c*]pyrans 3 and Separation of

Products: A 250-mL stainless steel autoclave was charged in the presence of air with PdI_2, KI (10 mmol per mmol of PdI_2) and a solution of **1** in MeOH (0.22 mmol of **1** per mL of MeOH). While stirring, the autoclave was pressurized with CO (up to 1.6 Mpa; up to 3.2 MPa in the case of **1a**) and air (up to 2.0 Mpa; up to 4.0 MPa in the case of **1a**), then heated at the required temperature for the required time. After cooling, the autoclave was degassed, the solvent evaporated under reduced pressure and products were separated by column chromatography (SiO_2): **7a**, (*E*)-**2a** and (*Z*)-**2a** were eluted in this order using hexane/EtOAc (90:10) as eluent; **3b** and (*E*)-**2b** were eluted in this order using hexane/EtOAc (98:2); **3c**, (*E*)-**2c**, (*Z*)-**2c** were eluted in this order using hexane/EtOAc (from 98:2 to 90:10); **3d** and (*E*)-**2d** were eluted in this order using hexane/EtOAc (99:1); **3e**, (*E*)-**2e** and (*Z*)-**2e** were eluted in this order using hexane/EtOAc (99:1); (*E*)-**2f** was purified using hexane/EtOAc (98:2); (*E*)-**2g** and (*Z*)-**2g** were eluted in this order using hexane/EtOAc (98:2). All products were characterised by spectroscopic techniques and elemental analyses as reported below.

Carbonylation of 1a: According to the general procedure, using 1.6 mg of PdI_2 (4.4×10^{-3} mmol), 7.3 mg of KI (0.044 mmol), 590 mg of **1a** (4.47 mmol) and 20.3 mL of MeOH at $T = 70$ °C, p(CO) = 3.2 MPa, p(air) = 0.8 MPa for 7 h, gave 390 mg of (*E*)-**2a** (46%), 68 mg of (*Z*)-**2a** (8%), and 109 mg of **7a** (11%).

(*E*)-1-(Methoxycarbonylmethylene)-1,3-dihydroisobenzofuran [(*E*)-2a]: Colourless solid, m.p. 51−53 °C. IR (KBr): $\tilde{\nu}$ = 1701 cm^{-1} (s), 1630 (vs), 1209 (m), 1148 (w), 1087 (vs), 835 (w), 769 (w), 718 (m). ^{1}H NMR ([D$_6$]acetone): δ = 9.25−9.21 (m, 1 H, 7-H), 7.62−7.46 (m, 3 H, aromatic), 5.55 (t, J = 1.0 Hz, 1 H, =CH), 5.43−5.41 (m, 2 H, OCH_2), 3.67 (s, 3 H, CO_2Me) ppm. ^{13}C NMR ([D$_6$]acetone): δ = 172.1, 168.1, 145.3, 132.4, 131.5, 128.9, 128.7, 121.9, 91.0, 74.7, 50.9 ppm. MS: m/z = 190 (47) [M^+], 159 (100), 132 (35), 131 (30), 103 (62), 102 (19), 77 (37). $C_{11}H_{10}O_3$ (190.06): calcd. C 69.46, H 5.30; found C 69.71, H 5.32.

(*Z*)-1-(Methoxycarbonylmethylene)-1,3-dihydroisobenzofuran [(*Z*)-2a]: Colourless solid, m.p. 115−117 °C. IR (KBr): $\tilde{\nu}$ = 1714 cm^{-1} (s), 1629 (vs), 1336 (w), 1295 (m), 1143 (vs), 1066 (s), 1001 (m), 767 (m). ^{1}H NMR ([D$_6$]acetone): δ = 7.81−7.77 (m, 1 H, aromatic), 7.58−7.43 (m, 3 H, aromatic), 5.55−5.53 (m, 3 H, =CH + OCH_2), 3.65 (s, 3 H, CO_2Me) ppm. ^{13}C NMR ([D$_6$]acetone): δ = 168.7, 166.3, 142.8, 133.7, 132.1, 129.3, 122.5, 122.3, 85.8, 77.1, 50.6 ppm. MS: m/z = 190 (41) [M^+], 159 (100), 132 (33), 131 (29), 103 (59), 102 (18), 77 (34). $C_{11}H_{10}O_3$ (190.06): calcd. C 69.46, H 5.30; found C 69.69, H 5.31.

Methyl (1-Methoxy-1,3-dihydroisobenzofuran-1-yl)acetate (7a): Pale yellow oil. IR (KBr): $\tilde{\nu}$ = 2950 cm^{-1} (m), 2868 (w), 1741 (s), 1359 (m), 1135 (m), 1100 (m), 1015 (m), 771 (w). ^{1}H NMR ([D$_6$]acetone): δ = 7.44−7.30 (m, 4 H, aromatic), 5.14 (distorted d, J = 12.7 Hz, 1 H, OC*H*H), 5.04 (distorted dd, J = 12.7, 1.0 Hz, 1 H, OCH*H*), 3.45 (s, 3 H, CO_2Me), 3.09 (distorted d, J = 15.1 Hz, 1 H, C*H*HCO_2Me), 3.00 (distorted d, J = 15.1 Hz, 1 H, CH*H*CO_2Me), 2.86 (s, 3 H, OMe) ppm. ^{13}C NMR ([D$_6$]acetone): δ = 169.5, 141.8, 137.9, 129.9, 128.4, 123.6, 121.7, 73.6, 51.3, 49.4, 45.0 ppm. MS: m/z = 222 (absent) [M^+], 191 (33), 190 (31), 149 (100), 131 (21), 119 (13), 103 (17), 91 (22), 77 (16). $C_{12}H_{14}O_4$ (222.10): calcd. C 64.85, H 6.35; found C 64.67, H 6.34.

Carbonylation of 1a′: According to the general procedure, using 2.5 mg of PdI_2 (6.9×10^{-3} mmol), 11.8 mg of KI (0.071 mmol), 710 mg of **1a′** (3.47 mmol) and 15.8 mL of MeOH at $T = 80$ °C, p(CO) = 1.6 MPa, p(air) = 0.4 MPa for 15 h, gave 46 mg of (*E*)-**2a** (7%), 290 mg of (*Z*)-**2a** (44%), and 77 mg of **7a** (10%).

Carbonylation of 1b: According to the general procedure, using 9.6 mg of PdI_2 (0.027 mmol), 44.1 mg of KI (0.27 mmol), 503 mg of **1b** (2.67 mmol) and 12.1 mL of MeOH at $T = 80$ °C, p(CO) = 1.6 MPa, p(air) = 0.4 MPa for 8 h, gave 158 mg of (*E*)-**2b** (24%), and 237 mg of **3b** (36%).

(*E*)-1-[(Butyl)(methoxycarbonyl)methylene]-1,3-dihydroisobenzofuran [(*E*)-2b]: Colourless oil. IR (film): $\tilde{\nu}$ = 2953 cm^{-1} (m), 2924 (m), 2869 (m), 1701 (s), 1608 (s), 1462 (w), 1274 (m), 1211 (m), 1117 (m), 1094 (m), 1067 (m), 765 (m), 721 (w). ^{1}H NMR ([D$_6$]acetone): δ = 8.78−8.73 (m, 1 H, 7-H), 7.48−7.36 (m, 3 H, aromatic), 5.37 (s, 2 H, OCH_2), 3.76 (s, 3 H, CO_2Me), 2.58−2.51 (m, 2 H, CH_2CH_2CH_2CH_3), 1.54−1.29 (m, 4 H, CH_2CH_2CH_2CH_3), 0.92 (t, J = 7.3 Hz, 3 H, CH_2CH_3) ppm. ^{13}C NMR ([D$_6$]acetone): δ = 169.2, 165.8, 144.5, 132.0, 131.0, 128.5, 127.7, 121.7, 106.0, 73.9, 51.3, 32.2, 28.5, 23.3, 14.3 ppm. MS: m/z = 246 (19) [M^+], 215 (12), 204 (13), 203 (100), 159 (16), 149 (38), 145 (18), 115 (23), 91 (11). $C_{15}H_{18}O_3$ (246.13): calcd. C 73.15, H 7.37; found C 73.31, H 7.35.

3-Butyl-4-(methoxycarbonyl)benzo[*c*]pyran (3b): Pale yellow oil. IR (film): $\tilde{\nu}$ = 2955 cm^{-1} (m), 2932 (w), 2861 (w), 1713 (s), 1603 (m), 1489 (w), 1454 (w), 1433 (w), 1333 (m), 1219 (m), 1119 (m), 1058 (s), 781 (w), 751 (w). ^{1}H NMR ([D$_6$]acetone): δ = 7.61−7.57 (m, 1 H, aromatic), 7.30−7.23 (m, 1 H, aromatic), 7.18 (td, J = 7.3, 1.3 Hz, 1 H, aromatic), 7.14−7.08 (m, 1 H, aromatic), 5.02 (s, 2 H, OCH_2), 3.81 (s, 3 H, CO_2Me), 2.60−2.53 (m, 2 H, CH_2CH_2CH_2CH_3), 1.66−1.54 (m, 2 H, CH_2CH_2CH_2CH_3), 1.44−1.31 (m, 2 H, CH_2CH_2CH_2CH_3), 0.91 (t, J = 7.3 Hz, 3 H, CH_2CH_3) ppm. ^{13}C NMR ([D$_6$]acetone): δ = 168.0, 167.7, 130.4, 128.9, 128.1, 127.2, 124.7, 123.7, 109.0, 69.5, 51.5, 33.1, 30.7, 23.1, 14.1 ppm. MS: m/z = 246 (58) [M^+], 215 (18), 189 (18), 185 (28), 162 (32), 161 (18), 145 (100), 131 (15), 129 (19), 117 (18), 116 (15), 115 (39), 103 (17), 102 (24). $C_{15}H_{18}O_3$ (246.13): calcd. C 73.15, H 7.37; found C 73.28, H 7.39.

Carbonylation of 1c: According to the general procedure, using 10.7 mg of PdI_2 (0.030 mmol), 49.3 mg of KI (0.30 mmol), 615 mg of **1c** (2.95 mmol) and 13.4 mL of MeOH at $T = 100$ °C, p(CO) = 1.6 MPa, p(air) = 0.4 MPa for 7 h, gave 118 mg of (*E*)-**2c** (15%), 173 mg of (*Z*)-**2c** (22%) and 196 mg of **3c** (25%).

(*E*)-1-[(Methoxycarbonyl)(phenyl)methylene]-1,3-dihydroisobenzofuran [(*E*)-2c]: Yellow oil. IR (film): $\tilde{\nu}$ = 1701 cm^{-1} (s), 1593 (s), 1463 (w), 1433 (w), 1295 (m), 1281 (m), 1240 (m), 1209 (m), 1081 (s), 763 (m). ^{1}H NMR ([D$_6$]acetone): δ = 8.40 (d, J = 7.8 Hz, 1 H, 7-H), 7.55−7.20 (m, 8 H, aromatic), 5.37 (s, 2 H, OCH_2), 3.70 (s, 3 H, CO_2Me) ppm. ^{13}C NMR ([D$_6$]acetone): δ = 169.3, 163.5, 144.3, 137.4, 131.5, 130.5, 128.9, 128.6, 127.2, 126.7, 123.4, 122.2, 107.1, 74.6, 51.9 ppm. MS: m/z = 266 (100) [M^+], 235 (24), 207 (29), 206 (14), 179 (33), 178 (68), 176 (17), 149 (50), 89 (21). $C_{17}H_{14}O_3$ (266.09): calcd. C 76.68, H 5.30; found C 76.81, H 5.33.

(*Z*)-1-[(Methoxycarbonyl)(phenyl)methylene]-1,3-dihydroisobenzofuran [(*Z*)-2c]: Colourless solid, m.p. 120−122 °C. IR (KBr): $\tilde{\nu}$ = 1699 cm^{-1} (s), 1607 (s), 1466 (w), 1430 (w), 1315 (w), 1281 (w), 1239 (m), 1205 (m), 1093 (s), 769 (m). ^{1}H NMR ([D$_6$]acetone): δ = 7.52−7.35 (m, 4 H, aromatic), 7.32−7.26 (m, 2 H, aromatic), 7.05−6.98 (m, 1 H, aromatic), 6.00 (d, J = 8.3 Hz, 1 H, aromatic), 5.52 (s, 2 H, OCH_2), 3.61 (s, 3 H, CO_2Me) ppm. ^{13}C NMR ([D$_6$]acetone): δ = 167.0, 165.0, 144.1, 137.1, 133.6, 132.4, 131.3, 129.6, 128.45, 128.41, 126.0, 122.3, 105.0, 75.6, 51.2 ppm. MS: m/z = 266 (100) [M^+], 235 (23), 207 (33), 206 (16), 179 (32), 178 (73), 176 (18), 149 (56), 89 (23). $C_{17}H_{14}O_3$ (266.09): calcd. C 76.68, H 5.30; found C 76.51, H 5.32.

4-(Methoxycarbonyl)-3-phenylbenzo[*c*]pyran (3c): Colourless solid, m.p. 100−102 °C. IR (KBr): $\tilde{\nu}$ = 1703 cm^{-1} (s), 1594 (m), 1559 (m), 1482 (m), 1331 (s), 1217 (s), 1035 (m), 975 (w), 765 (s), 699 (m). ^1H NMR ([D$_6$]acetone): δ = 7.89 (d, *J* = 7.6 Hz, 1 H), 7.59−7.39 (m, 5 H, aromatic), 7.35 (td, *J* = 7.4, 1.6 Hz, 1 H), 7.31−7.20 (m, 2 H, aromatic), 5.26 (s, 2 H, OCH_2), 3.52 (s, 3 H, CO_2Me) ppm. ^{13}C NMR ([D$_6$]acetone): δ = 168.8, 161.2, 135.5, 131.0, 130.1, 129.6, 129.1, 128.9, 128.0, 127.8, 124.9, 123.0, 109.7, 70.2, 51.7 ppm. MS: *m*/*z* = 266 (100) [M$^+$], 235 (14), 234 (22), 207 (17), 206 (15), 205 (27), 179 (36), 178 (77), 105 (25), 77 (37). $C_{17}H_{14}O_3$ (266.09): calcd. C 76.68, H 5.30; found C 76.81, H 5.30.

Carbonylation of 1d: According to the general procedure, using 10.7 mg of PdI_2 (0.030 mmol), 49.5 mg of KI (0.30 mmol), 732 mg of **1d** (3.00 mmol) and 13.6 mL of MeOH at *T* = 80 °C, *p*(CO) = 1.6 MPa, *p*(air) = 0.4 MPa for 2 h, gave 336 mg of (*E*)-**2d** (37%), and 154 mg of **3d** (17%).

(*E*)-3-Butyl-1-[(butyl)(methoxycarbonyl)methylene]-1,3-dihydroisobenzofuran [(*E*)-2d]: Colourless oil. IR (film): $\tilde{\nu}$ = 2955 cm^{-1} (m), 2931 (m), 2860 (w), 1701 (s), 1611 (m), 1598 (m), 1462 (w), 1272 (m), 1209 (m), 1118 (m), 1097 (m), 1070 (s), 763 (s). ^1H NMR ([D$_6$]acetone): δ = 8.76 (d, *J* = 7.8 Hz, 1 H, 7-H), 7.52−7.36 (m, 3 H, aromatic), 5.54 (dd, J = 7.8, 3.9 Hz, 1 H, OCH), 3.76 (s, 3 H, CO_2Me), 2.65−2.48 (m, 2 H, =CC*H*$_2$), 2.11−1.98 (m, 1 H, OCHC*H*H), 1.75−1.59 (m, 1 H, OCHCH*H*), 1.58−1.30 (m, 8 H, 2 $CH_2CH_2CH_3$), 0.93 (t, *J* = 7.1 Hz, 3 H, Me), 0.90 (t, *J* = 7.1 Hz, 3 H, Me) ppm. ^{13}C NMR ([D$_6$]acetone): δ = 169.3, 165.1, 147.8, 132.3, 131.1, 128.7, 128.0, 121.8, 105.8, 84.8, 51.3, 36.0, 32.2, 28.5, 27.7, 23.3, 23.2 ppm. MS: *m*/*z* = 302 (37) [M$^+$], 271 (20), 259 (100), 245 (33), 227 (66), 215 (29), 201 (30), 185 (34), 171 (57), 157 (35), 145 (31), 131 (23), 115 (41). $C_{19}H_{26}O_3$ (302.19): calcd. C 75.46, H 8.67; found C 75.58, H 8.65.

1,3-Dibutyl-4-(methoxycarbonyl)benzo[*c*]pyran (3d): Pale yellow oil. IR (film): $\tilde{\nu}$ = 2954 cm^{-1} (m), 2931 (m), 1711 (s), 1601 (m), 1488 (w), 1453 (w), 1432 (w), 1205 (m), 1185 (m), 1125 (m), 1103 (m), 1054 (s), 751 (m). ^1H NMR ([D$_6$]acetone): δ = 7.58−7.53 (m, 1 H, aromatic), 7.25 (td, *J* = 7.3, 1.5 Hz, 1 H, aromatic), 7.20 (td, *J* = 7.3, 1.5 Hz, 1 H, aromatic), 7.14−7.09 (m, 1 H, aromatic), 5.12 (dd, *J* = 8.3, 4.9 Hz, 1 H, OCH), 3.82 (s, 3 H, CO_2Me), 2.66−2.46 (m, 2 H, =CCH_2), 2.02−1.87 (m, 1 H, OCHC*H*H), 1.82−1.30 (m, 9 H, OCHCH*H* + 2 $CH_2CH_2CH_3$), 0.93 (t, *J* = 7.3 Hz, 3 H, Me), 0.92 (t, *J* = 7.1 Hz, 3 H, Me) ppm. ^{13}C NMR ([D$_6$]acetone): δ = 168.1, 164.8, 131.5, 129.2, 128.5, 127.1, 124.8, 124.0, 108.1, 79.0, 51.5, 34.1, 33.2, 30.5, 28.2, 23.1, 14.27, 14.13 ppm. MS: *m*/*z* = 302 (9) [M$^+$], 246 (17), 245 (100), 115 (9). $C_{19}H_{26}O_3$ (302.19): calcd. C 75.46, H 8.67; found C 75.35, H 8.69.

Carbonylation of 1e: According to the general procedure, using 11.4 mg of PdI_2 (0.032 mmol), 52.8 mg of KI (0.32 mmol), 818 mg of **1e** (3.1 mmol) and 14.0 mL of MeOH at *T* = 80 °C, *p*(CO) = 1.6 MPa, *p*(air) = 0.4 MPa for 7 h, gave 450 mg of (*E*)-**2e** (45%), 60 mg of (*Z*)-**2e** (6%) and 100 mg of **3e** (10%).

(*E*)-3-Butyl-1-[(methoxycarbonyl)(phenyl)methylene]-1,3-dihydroisobenzofuran [(*E*)-2e]: Viscous yellow oil. IR (film): $\tilde{\nu}$ = 1703 cm^{-1} (s), 1593 (s), 1463 (w), 1432 (w), 1295 (m), 1235 (m), 1202 (m), 1091 (s), 761 (m). ^1H NMR ([D$_6$]acetone): δ = 8.39−8.34 (m, 1 H, 7-H), 7.55−7.41 (m, 5 H, aromatic), 7.38−7.31 (m, 2 H, aromatic), 7.26−7.19 (m, 1 H, aromatic), 5.52 (dd, *J* = 7.8, 3.9 Hz, 1 H, OCH), 3.75 (s, 3 H, CO_2Me), 2.06−1.92 (m, 1 H, OCHC*H*H), 1.76−1.62 (m, 1 H, OCHCH*H*), 1.43−1.20 (m, 4 H, $CH_2CH_2CH_3$), 0.85 (t, 3 H, 7.1, Me) ppm. ^{13}C NMR ([D$_6$]acetone): δ = 169.4, 162.4, 147.3, 137.4, 132.3, 131.4, 130.4, 129.0, 128.6, 127.1, 126.6, 122.1, 106.7, 85.6, 51.9, 35.7, 27.6, 23.0, 14.2 ppm. MS: *m*/*z* = 322 (89) [M$^+$], 291 (14), 265 (100), 237 (18), 233 (21), 220 (21), 219 (17), 207 (21), 206 (31), 205 (48), 178 (37), 115 (23), 91 (23), 77 (18). $C_{21}H_{22}O_3$ (322.16): calcd. C 78.23, H 6.88; found C 78.15, H 6.90.

(*Z*)-3-Butyl-1-[(methoxycarbonyl)(phenyl)methylene]-1,3-dihydroisobenzofuran [(*Z*)-2e]: Colourless solid, 74−77 °C. IR (KBr): $\tilde{\nu}$ = 1674 cm^{-1} (s), 1618 (m), 1600 (m), 1463 (w), 1435 (m), 1359 (m), 1242 (m), 1100 (m), 774 (m), 713 (m). ^1H NMR ([D$_6$]acetone): δ = 7.50−7.36 (m, 5 H, aromatic), 7.33−7.26 (m, 2 H, aromatic), 7.06−6.99 (m, 1 H, aromatic), 5.99 (d, *J* = 7.8 Hz, 1 H, aromatic), 5.68 (dd, *J* = 7.8, 3.9 Hz, 1 H, OCH), 3.62 (s, 3 H, CO_2Me), 2.16−2.03 (m, 1 H, OCHC*H*H), 1.80−1.66 (m, 1 H, OCHCH*H*), 1.60−1.35 (m, 4 H, $CH_2CH_2CH_3$), 0.93 (t, *J* = 7.3 Hz, 3 H, Me) ppm. ^{13}C NMR ([D$_6$]acetone): δ = 167.0, 164.2, 147.4, 137.2, 133.8, 132.4, 131.3, 129.6, 128.6, 128.4, 126.0, 122.2, 105.0, 86.9, 51.1, 35.9, 27.8, 23.1, 14.3 ppm. MS: *m*/*z* = 322 (100) [M$^+$], 291 (13), 265 (86), 206 (22), 205 (33), 178 (23). $C_{21}H_{22}O_3$ (322.16): calcd. C 78.23, H 6.88; found C 78.35, H 6.89.

1-Butyl-4-(methoxycarbonyl)-3-phenylbenzo[*c*]pyran (3e): Yellow oil. IR (film): $\tilde{\nu}$ = 2953 cm^{-1} (m), 1713 (s), 1598 (m), 1486 (m), 1452 (w), 1433 (w), 1216 (m), 1103 (s), 1036 (m), 761 (s), 698 (m). ^1H NMR ([D$_6$]acetone): δ = 7.90−7.85 (m, 1 H, aromatic), 7.59−7.53 (m, 2 H, aromatic), 7.49−7.43 (m, 3 H, aromatic), 7.34 (td, *J* = 7.3, 1.5 Hz, 1 H, aromatic), 7.28 (td, *J* = 7.3, 1.5 Hz, 1 H, aromatic), 7.21 (distorted dd, *J* = 7.3, 1.5 Hz, 1 H), 5.31 (dd, *J* = 8.3, 5.4 Hz, 1 H, OCH), 3.51 (s, 3 H, CO_2Me), 2.19−2.02 (m, 1 H, OCHC*H*H), 2.01−1.87 (m, 1 H, OCHCH*H*), 1.76−1.60 (m, 1 H, $OCHCH_2CHH$), 1.59−1.34 (m, 3 H, $OCHCH_2CHH$ + CH_2CH_3), 0.94 (t, *J* = 7.3 Hz, 3 H, CH_2CH_3) ppm. ^{13}C NMR ([D$_6$]acetone): δ = 168.9, 158.8, 136.0, 131.3, 130.8, 129.4, 129.1, 129.0, 128.8, 127.8, 124.9, 123.2, 108.9, 79.6, 51.8, 33.7, 28.2, 23.2, 14.3 ppm. MS: *m*/*z* = 322 (11) [M$^+$], 291 (2), 266 (19), 265 (100), 205 (21), 105 (16), 77 (13). $C_{21}H_{22}O_3$ (322.16): calcd. C 78.23, H 6.88; found C 78.19, H 6.85.

Carbonylation of 1f: According to the general procedure, using 1.2 mg of PdI_2 (3.3 × 10^{-3} mmol), 5.6 mg of KI (0.034 mmol), 823 mg of **1f** (3.4 mmol) and 15.3 mL of MeOH at *T* = 80 °C, *p*(CO) = 1.6 MPa, *p*(air) = 0.4 MPa for 2 h, gave 720 mg of (*E*)-**2f** (70%).

(*E*)-1,1-Diethyl-1-[(butyl)(methoxycarbonyl)methylene]-1,3-dihydroisobenzofuran [(*E*)-2f]: Pale yellow oil. IR (film): $\tilde{\nu}$ = 2968 cm^{-1} (m), 2935 (m), 2874 (w), 1699 (s), 1610 (s), 1597 (s), 1461 (m), 1273 (m), 1093 (s), 1066 (s), 957 (m), 765 (m). ^1H NMR ([D$_6$]acetone): δ = 8.83−8.78 (m, 1 H, 7-H), 7.47 (td, *J* = 7.3, 1.0 Hz, 1 H, aromatic), 7.42−7.35 (m, 1 H, aromatic), 7.34−7.29 (m, 1 H, aromatic), 3.74 (s, 3 H, CO_2Me), 2.62−2.55 (m, 2 H, =CCH_2), 2.09−1.83 [m, 4 H, $OC(CH_2CH_3)_2$], 1.58−1.31 (m, 4 H, $CH_2CH_2CH_3$), 0.93 (t, *J* = 7.3 Hz, 3 H, $CH_2CH_2CH_3$), 0.63 [t, *J* = 7.3 Hz, 6 H, $OC(CH_2CH_3)_2$] ppm. ^{13}C NMR ([D$_6$]acetone): δ = 169.3, 165.2, 149.0, 133.5, 131.1, 128.6, 127.9, 121.4, 105.2, 92.9, 51.1, 33.0, 32.0, 28.5, 23.2, 14.3, 7.8 ppm. MS: *m*/*z* = 302 (11) [M$^+$], 274 (20), 273 (100), 259 (24), 227 (16), 213 (14), 185 (12), 181 (17), 171 (13), 128 (12), 115 (13). $C_{19}H_{26}O_3$ (302.19): calcd. C 75.46, H 8.67; found C 75.66, H 8.68.

Carbonylation of 1g: According to the general procedure, using 1.2 mg of PdI_2 (3.3 × 10^{-3} mmol), 5.7 mg of KI (0.034 mmol), 884 mg of **1g** (3.3 mmol) and 15.2 mL of MeOH at *T* = 80 °C, *p*(CO) = 1.6 MPa, *p*(air) = 0.4 MPa for 2 h, gave 532 mg of (*E*)-**2g** (50%), and 191 mg of (*Z*)-**2g** (18%).

(*E*)-1,1-Diethyl-1-[(methoxycarbonyl)(phenyl)methylene]-1,3-dihydroisobenzofuran [(*E*)-2g]: Pale yellow solid, 57−58 °C. IR

(KBr): $\tilde{\nu}$ = 1698 cm^{-1} (s), 1593 (s), 1460 (m), 1433 (m), 1361 (w), 1297 (m), 1235 (m), 1131 (m), 1079 (vs), 961 (m), 765 (m), 753 (m), 701 (m). ^1H NMR ([D$_6$]acetone): δ = 8.45−8.39 (m, 1 H, 7-H, aromatic), 7.55−7.29 (m, 7 H, aromatic), 7.25−7.18 (m, 1 H, aromatic), 3.72 (s, 3 H, CO_2Me), 1.99−1.80 (m, 4 H, 2 CH_2CH_3), 0.61 (t, *J* = 7.3 Hz, 6 H, 2 CH_2CH_3) ppm. ^{13}C NMR ([D$_6$]acetone): δ = 169.4, 162.6, 148.6, 137.6, 132.4, 131.5, 130.3, 128.9, 128.6, 127.0, 126.6, 121.7, 106.1, 94.2, 51.8, 32.8, 7.9 ppm. MS: *m*/*z* = 322 (30) [M^+], 294 (21), 293 (100), 237 (6), 233 (6), 205 (8), 176 (6). $C_{21}H_{22}O_3$ (322.16): calcd. C 78.23, H 6.88; found C 78.33, H 6.86.

(*Z*)-1,1-Diethyl-1-[(methoxycarbonyl)(phenyl)methylene]-1,3-dihydroisobenzofuran [(*Z*)-2g]: Colourless solid, 114−116 °C. IR (KBr): $\tilde{\nu}$ = 1671 cm^{-1} (s), 1613 (m), 1598 (w), 1463 (w), 1434 (w), 1233 (s), 1103 (m), 1091 (m), 1013 (m), 770 (m), 753 (m), 713 (m). ^1H NMR ([D$_6$]acetone): δ = 7.50−7.35 (m, 5 H, aromatic), 7.32−7.26 (m, 2 H, aromatic), 7.06−6.99 (m, 1 H, aromatic), 6.02−5.97 (m, 1 H, aromatic), 3.61 (s, 3 H, CO_2Me), 2.18−2.03 (m, 2 H, 2 C*H*HCH_3), 2.03−1.89 (m, 2 H, CH*H*CH_3), 0.71 (t, J = 7.3 Hz, 6 H, 2 CH_2CH_3) ppm. ^{13}C NMR ([D$_6$]acetone): δ = 167.0, 164.4, 148.8, 137.3, 135.0, 132.5, 131.4, 129.6, 128.5, 128.4, 125.9, 122.0, 104.4, 95.5, 51.1, 32.9, 7.9 ppm. MS: *m*/*z* = 322 (28) [M^+], 294 (20), 293 (100), 233 (6), 205 (8), 176 (7). $C_{21}H_{22}O_3$ (322.16): calcd. C 78.23, H 6.88; found C 78.19, H 6.87.

Typical Procedure for Oxidative Carbonylation of 2-Alkynyl Benzaldehydes and 2-Alkynylphenyl Ketones 4 to 1-(Alkoxycarbonyl)methylene-1,3-dihydroisobenzofurans 5 and 4-(Alkoxycarbonyl)benzo[*c*-]pyrans 6 and Separation of Products: A 45-mL stainless steel autoclave was charged in the presence of air with PdI_2, KI (10 mmol per mmol of PdI_2) and a solution of **4** in MeOH or an MeCN/MeOH mixture (0.34−0.38 mmol of **4** per mL of solvent). The autoclave was pressurized with stirring at room temperature with CO (up to 2.4 MPa) and air (up to 3.2 MPa), then heated at the required temperature for the required time. After cooling, the autoclave was degassed, the solvent evaporated under reduced pressure and products were separated by column chromatography (SiO_2): (*E*)-**5a** and (*Z*)-**5a** (R^4 = Me) were eluted in this order using hexane/EtOAc (4:1) as eluent; (*E*)-**5a′** and (*Z*)-**5a′** (R^4 = *i*Pr) were eluted in this order using CH_2Cl_2/acetone (9:1) as eluent; **6b**, (*E*)-**5b** and (*Z*)-**5b** were eluted in this order using hexane/EtOAc (from 6:1 to 4:1); (*E*)-**5c** and (*Z*)-**5c** were eluted in this order using hexane/EtOAc (from 15:1 to 10:1); **6d** and (*E*)-**5d** were eluted in this order using hexane/acetone (5:1); (*E*)-**5e** was purified using hexane/CH_2Cl_2/acetone (14:5:1); **6f** was purified using hexane/acetone (10:1); (*Z*)-**5g** was purified using hexane/EtOAc (18:1); **6h** and (*E*)-**5h** were eluted in this order using hexane/EtOAc (20:1); (*E*)-**5i** and (*Z*)-**5i** were eluted in this order using hexane/EtOAc (10:1). Spectroscopic data of products **9d**, **9f** and **9h** agree with those already reported.[6] All other products were characterised by spectroscopic techniques and elemental analyses as detailed below.

Carbonylation of 4a with MeOH: According to the general procedure, using 24.0 mg of PdI_2 (6.7×10^{-2} mmol), 111.0 mg of KI (0.67 mmol), 288 mg of **4a** (2.00 mmol) and a mixture of 5 mL MeCN and 0.4 mL of MeOH at *T* = 80 °C, *p*(CO) = 2.4 MPa, *p*(air) = 0.8 MPa for 48 h, gave 234 mg of (*E*)-**5a** (50%) and 75 mg of (*Z*)-**5a** (16%).

(*E*)-3-Methoxy-1-[(methoxycarbonyl)methylene]-3-methyl-1,3-dihydroisobenzofuran [(*E*)-5a]: Colourless oil. IR (film): $\tilde{\nu}$ = 3115 cm^{-1} (w), 3075 (w), 2994 (m), 2949 (m), 2834 (w), 1711 (s), 1637 (s), 1467 (s), 1377 (s), 1231 (m), 1178 (s), 1121 (s), 947 (m), 862 (m), 766 (m). ^1H NMR ($CDCl_3$): δ = 9.11 (m, 1 H, 7-H), 7.58−7.51 (m, 2 H, aromatic), 7.39−7.36 (m, 1 H, aromatic), 5.73 (s, 1 H, =CH), 3.76 (s, 3 H, CO_2CH_3), 2.96 (s, 3 H, OCH_3), 1.75 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 167.8, 166.7, 143.3, 131.7, 131.5, 129.9, 128.0, 121.6, 111.2, 92.5, 50.9, 50.8, 25.5 ppm. MS: *m*/*z* = 234 (20) [M^+], 219 (50), 205 (1), 203 (50), 187 (15), 175 (100), 159 (30), 144 (20), 129 (20), 115 (50), 103 (15), 91 (15), 77 (15), 59 (10). $C_{13}H_{14}O_4$ (234.09): calcd. C 66.66, H 6.02; found C 66.55, H 6.01.

(*Z*)-3-Methoxy-1-[(methoxycarbonyl)methylene]-3-methyl-1,3-dihydroisobenzofuran [(*Z*)-5a]: Colourless oil. IR (film): $\tilde{\nu}$ = 2964 cm^{-1} (s), 2907 (w), 1714 (s), 1653 (s), 1262 (s), 1082 (s), 1037 (s), 875 (m), 803 (s). ^1H NMR ($CDCl_3$): δ = 7.59−7.46 (m, 3 H, aromatic), 7.41 (d, *J* = 7.3 Hz, 1 H, aromatic), 5.50 (s, 1 H, =CH), 3.78 (s, 3 H, CO_2CH_3), 3.02 (s, 3 H, OCH_3), 1.85 (s, 3 H, CH_3) ppm; the NOESY tp spectrum shows the presence of an interaction between a vinyl proton (δ = 5.50 ppm) and an aromatic proton (δ = 7.59−7.46 ppm). ^{13}C NMR ($CDCl_3$): δ = 166.1, 163.5, 141.5, 133.8, 131.5, 130.0, 122.2, 121.2, 114.7, 86.5, 51.0, 50.9, 25.5 ppm. MS: *m*/*z* = 234 (20) [M^+], 219 (50), 205 (1), 203 (50), 187 (15), 175 (100), 159 (30), 144 (20), 129 (20), 115 (50), 103 (15), 91 (15), 77 (15), 59 (10). $C_{13}H_{14}O_4$ (234.09): calcd. C 66.66, H 6.02; found C 66.59, H 6.00.

Carbonylation of 4a with *i*PrOH: According to the general procedure, using 24.0 mg of PdI_2 (6.7×10^{-2} mmol), 111.0 mg of KI (0.67 mmol), 288 mg of **4a** (2.00 mmol) and a mixture of 5 mL of MeCN and 0.8 mL of *i*PrOH at *T* = 80 °C, *p*(CO) = 2.4 MPa, *p*(air) = 0.8 MPa for 48 h, gave 162 mg of (*E*)-**5a′** (28%), and 168 mg of (*Z*)-**5a′** (29%).

(*E*)-3-Isopropoxy-1-[(isopropoxycarbonyl)methylene]-3-methyl-1,3-dihydroisobenzofuran [(*E*)-5a′]: Pale yellow oil. IR (film): $\tilde{\nu}$ = 3079 cm^{-1} (w), 2993 (s), 2948 (s), 1712 (s), 1639 (s), 1465 (s), 1377 (s), 1235 (m), 1179 (s), 1124 (s), 945 (m), 766 (m). ^1H NMR ($CDCl_3$): δ = 9.13−9.10 (m, 1 H, 7-H), 7.53−7.49 (m, 2 H, aromatic), 7.39−7.36 (m, 1 H, aromatic), 5.65 (s, 1 H, =CH), 5.09 [m, 1 H, C*H*$(CH_3)_2$], 3.32 [m, 1 H, C*H*$(CH_3)_2$], 1.71 (s, 3 H, CH_3), 1.31 (d, *J* = 6.3 Hz, 3 H, $CHCH_3CH_3$), 1.29 (d, *J* = 6.1 Hz, 3 H, $CHCH_3CH_3$), 1.13 (d, *J* = 6.1 Hz, 3 H, $CHCH_3CH_3$), 0.91 (d, *J* = 6.2 Hz, 3 H, $CHCH_3CH_3$) ppm. ^{13}C NMR ($CDCl_3$): δ = 167.1, 166.1, 144.5, 131.4, 129.7, 128.0, 121.7, 111.4, 102.9, 93.3, 67.0, 66.7, 26.6, 24.2, 23.4, 22.0 (2) ppm. MS: *m*/*z* = 290 (1) [M^+], 231 (10), 204 (9), 189 (10), 161 (100), 147 (22), 129 (10), 115 (13), 91 (10). $C_{17}H_{22}O_4$ (290.15): calcd. C 70.32, H 7.64; found C 70.26, H 7.62.

(*Z*)-3-Isopropoxy-1-[(isopropoxycarbonyl)methylene]-3-methyl-1,3-dihydroisobenzofuran [(*Z*)-5a′]: Yellow oil. IR (film): $\tilde{\nu}$ = 3059 cm^{-1} (w), 2975 (s), 1715 (s), 1648 (s), 1460 (s), 1367 (s), 1240 (m), 1165 (s), 1127 (s), 966 (m), 765 (m). ^1H NMR ($CDCl_3$): δ = 7.55−7.39 (m, 4 H, aromatic), 5.44 (s, 1 H, =CH), 5.16−5.08 [m, 1 H, C*H*$(CH_3)_2$], 3.42−3.34 [m, 1 H, C*H*$(CH_3)_2$], 1.81 (s, 3 H, CH_3), 1.30 (d, *J* = 6.3 Hz, 3 H, $CHCH_3CH_3$), 1.28 (d, *J* = 6.2 Hz, 3 H, $CHCH_3CH_3$), 1.20 (d, *J* = 6.1 Hz, 3 H, $CHCH_3CH_3$), 0.95 (d, *J* = 6.2 Hz, 3 H, $CHCH_3CH_3$) ppm. MS: *m*/*z* = 290 (2) [M^+], 231 (13), 204 (11), 189 (10), 161 (100), 147 (26), 129 (10), 115 (10), 91 (8). $C_{17}H_{22}O_4$ (290.15): calcd. C 70.32, H 7.64; found C 70.23, H 7.63.

Carbonylation of 4b: According to the general procedure, using 24.0 mg of PdI_2 (6.7×10^{-2} mmol), 111.0 mg of KI (0.67 mmol), 260 mg of **4b** (2.00 mmol) and a mixture of 5 mL MeCN and 0.2 mL of MeOH at *T* = 70 °C, *p*(CO) = 2.4 MPa, *p*(air) = 0.8 MPa for 24 h, gave 79 mg of (*E*)-**5b** (18%), 123 mg of (*Z*)-**5b** (28%), and 40 mg of **6b** (9%). The same reaction carried out in 5.2 mL of MeOH led to the maleic diester **9b** (341 mg, 58%).

(*E*)-3-Methoxy-1-[(methoxycarbonyl)methylene]-1,3-dihydroisobenzofuran [(*E*)-5b]: Pale yellow oil. IR (film): $\tilde{\nu}$ = 2948 cm^{-1} (m), 2843(w), 1713 (s), 1647 (s), 1428 (m), 1294 (s), 1208 (s), 1159 (s), 947 (m), 766 (m). ^1H NMR ($CDCl_3$): δ = 9.12−9.09 (m, 1 H, 7-H), 7.56−7.53 (m, 2 H, aromatic), 7.48−7.45 (m, 1 H, aromatic), 6.35 (s, 1 H, OCH), 5.74 (s, 1 H, =CH), 3.75 (s, 3 H, CO_2CH_3), 3.45 (s, 3 H, OCH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 167.7, 167.4, 140.9, 131.6, 131.4, 130.3, 128.0, 122.5, 106.0, 93.2, 54.7, 51.0 ppm. MS: *m*/*z* = 220 (10) [M^+], 189 (20), 173 (20), 161 (100), 145 (10), 130 (20), 115 (17), 102 (21), 89 (19), 77 (16), 59 (21). $C_{12}H_{12}O_4$ (220.07): calcd. C 65.45, H 5.49; found C 65.34, H 5.48.

(*Z*)-3-Methoxy-1-[(methoxycarbonyl)methylene]-1,3-dihydroisobenzofuran [(*Z*)-5b]: Pale yellow oil. IR (film): $\tilde{\nu}$ = 2950 cm^{-1} (m), 2846 (w), 1711 (s), 1650 (s), 1434 (m), 1293 (s), 1208 (s), 1158 (s), 951 (m) 770 (m). ^1H NMR ($CDCl_3$): δ = 7.58−7.46 (m, 4 H, aromatic), 6.54 (s, 1 H, OCH), 5.53 (s, 1 H, =CH), 3.76 (s, 3 H, CO_2CH_3), 3.57 (s, 3 H, OCH_3) ppm; the NOESY tp spectrum shows the presence of an interaction between a vinyl proton (δ = 5.53 ppm) and an aromatic proton (δ = 7.58−7.46 ppm). ^{13}C NMR ($CDCl_3$): δ = 166.1, 164.2, 139.0, 133.7, 131.4, 130.3, 123.1, 121.2, 108.9, 87.3, 55.7, 51.0 ppm. MS: *m*/*z* = 220 (10) [M^+], 205 (1), 189 (20), 173 (19), 161 (100), 145 (10), 130 (20), 115 (16), 102 (21), 89 (20), 77 (16), 59 (22). $C_{12}H_{12}O_4$ (220.07): calcd. C 65.45, H 5.49; found C 65.40, H 5.46.

1-Methoxy-4-(methoxycarbonyl)benzo[*c*]pyran (6b): Pale yellow oil. IR (film): $\tilde{\nu}$ = 2949 cm^{-1} (m), 2848 (w), 1710 (s), 1651 (s), 1440 (m), 1250 (m), 1208 (s), 1081 (s), 950 (m), 760 (m). ^1H NMR ($CDCl_3$): δ = 8.32 (br. d, *J* = 7.7 Hz, 1 H, aromatic), 7.78 (s, 1 H, CH), 7.44 (td, *J* = 7.8, 1.6 Hz, 1 H, aromatic), 7.32 (td, *J* = 7.5, 1.3 Hz, 1 H, aromatic), 7.23 (dd, *J* = 7.6, 1.6 Hz, 1 H, aromatic), 6.03 (s, 1 H, CH), 3.83 (s, 3 H, CO_2CH_3), 3.55 (s, 3 H, OCH_3) ppm. MS: *m*/*z* = 220 (38) [M^+], 189 (100), 173 (10), 161 (60), 145 (11), 132 (20), 118 (29), 102 (29), 89 (30), 77 (20), 59 (19). $C_{12}H_{12}O_4$ (220.07): calcd. C 65.45, H 5.49; found C 65.37, H 5.47.

Carbonylation of 4c: According to the general procedure, using 24.0 mg of PdI_2 (6.7×10^{-2} mmol), 111.0 mg of KI (0.67 mmol), 440 mg of **4c** (2.00 mmol) and 5.4 mL of MeOH at *T* = 85 °C, *p*(CO) = 2.4 MPa, *p*(air) = 0.8 MPa for 48 h, gave 81 mg (13%) of (*E*)-**5c** and 267 mg (43%) of (*Z*)-**5c**.

(*E*)-3-Methoxy-1-[(methoxycarbonyl)(phenyl)methylene]-3-methyl-1,3-dihydroisobenzofuran [(*E*)-5c]: Colourless solid, 96−99 °C. IR (KBr): $\tilde{\nu}$ = 2936 cm^{-1} (w), 1707 (s), 1598 (m), 1464 (w), 1297 (m), 1231 (m), 1175 (m), 1117 (m), 1063 (s), 761 (m). ^1H NMR ($CDCl_3$): δ = 8.27−8.24 (m, 1 H, 7-H), 7.51−7.35 (m, 7 H, aromatic), 7.29 (d, *J* = 7.1 Hz, 1 H, aromatic), 3.83 (s, 3 H, CO_2CH_3), 2.97 (s, 3 H, OCH_3), 1.72 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 169.1, 158.0, 142.5, 135.5, 132.2, 130.7, 129.8, 129.4 (2), 127.9, 126.8, 125.6, 121.9, 111.1, 107.5, 52.0, 50.7, 25.6 ppm. MS: *m*/*z* = 310 (40) [M^+], 295 (9), 279 (25), 251 (100), 235 (58), 219 (42), 207 (36), 189 (29), 176 (26), 161 (28), 139 (18), 129 (30), 105 (22), 89 (20), 77 (28), 59 (7). $C_{19}H_{18}O_4$ (310.12): calcd. C 73.53, H 5.85; found C 73.49, H 5.81.

(*Z*)-3-Methoxy-1-[(methoxycarbonyl)(phenyl)methylene]-3-methyl-1,3-dihydroisobenzofuran [(*Z*)-5c]: Colourless solid, 145−147 °C. IR (KBr): $\tilde{\nu}$ = 2943 cm^{-1} (w), 1707 (s), 1617 (s), 1278 (m), 1229 (s), 1180 (m), 1120 (m), 1067 (m), 1042 (s), 880 (m), 778 (m). ^1H NMR ($CDCl_3$): δ = 7.45−7.42 (m, 3 H, aromatic), 7.36−7.31 (m, 4 H, aromatic), 7.05 (ddd, *J* = 8.0, 6.3, 2.2 Hz, 1 H, aromatic), 6.00 (d, *J* = 8.0 Hz, 1 H, aromatic), 3.74 (s, 3 H, CO_2CH_3), 3.08 (s, 3 H, OCH_3), 1.87 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 166.8, 160.1, 142.7, 135.2, 133.6, 131.2 (2), 130.6, 129.3, 128.8 (2), 127.9, 125.3, 121.8, 112.3, 51.5, 50.8, 25.5 ppm (the missing C signal is hidden under either the one at δ = 112.3 or 135.2 ppm). MS: *m*/*z* = 310 (40) [M^+], 295 (9), 279 (25), 251 (100), 235 (58), 219 (42), 207 (36), 189 (29), 176 (26), 161 (28), 139 (18), 129 (30), 105 (22), 89 (20), 77 (20), 58 (6). $C_{19}H_{18}O_4$ (310.12): calcd. C 73.53, H 5.85; found C 73.42, H 5.83.

Carbonylation of 4d: According to the general procedure, using 24.0 mg of PdI_2 (6.7×10^{-2} mmol), 111.0 mg of KI (0.67 mmol), 412 mg of **4d** (2.00 mmol) and a mixture of 5 mL MeCN and 0.2 mL of MeOH at *T* = 85 °C, *p*(CO) = 2.4 MPa, *p*(air) = 0.8 MPa for 24 h, gave 12 mg of (*E*)-**5d** (2%), 237 mg of **6d** (40%) and 43 mg of **9d** (9%).

(*E*)-3-Methoxy-1-[(methoxycarbonyl)(phenyl)methylene]-1,3-dihydroisobenzofuran [(*E*)-5d]: Pale yellow oil. IR (film): $\tilde{\nu}$ = 2940 cm^{-1} (w), 1709 (s), 1607 (m), 1289 (m), 1184 (m), 1059 (s), 765 (m). ^1H NMR ($CDCl_3$): δ = 8.35−8.31 (m, 1 H, 7-H), 7.50−7.26 (m, 8 H, aromatic), 6.32 (s, 1 H, OCH), 3.82 (s, 3 H, CO_2CH_3), 3.40 (s, 3 H, OCH_3) ppm. MS: *m*/*z* = 296 (5) [M^+], 265 (9), 237 (100), 221 (13), 205 (65), 194 (9), 176 (22), 165 (30), 105 (18), 77 (31), 59 (16). $C_{18}H_{16}O_4$ (296.10): calcd. C 72.96, H 5.44; found C 72.86, H 5.40.

1-Methoxy-4-(methoxycarbonyl)-3-phenylbenzo[*c*]pyran (6d): Pale yellow oil. IR (film): $\tilde{\nu}$ = 3058 cm^{-1} (w), 2947 (m), 2832 (w), 1712 (s), 1605 (s), 1488 (m), 1336 (s), 1218 (s), 1099 (m), 1065 (s), 956 (m), 763 (s). ^1H NMR ($CDCl_3$): δ = 7.86 (br. d, *J* = 8.0 Hz, 1 H, aromatic), 7.60−7.57 (m, 2 H, aromatic), 7.48−7.41 (m, 4 H, aromatic), 7.37−7.29 (m, 2 H, aromatic), 6.12 (s, 1 H, OCH), 3.71 (s, 3 H, CO_2CH_3), 3.58 (s, 3 H, OCH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 168.2, 155.1, 135.1, 129.8, 129.6, 128.4 (2), 128.1 (2), 127.4, 127.2, 125.9, 125.7, 123.0, 108.3, 100.3, 56.0, 51.6 ppm. MS: *m*/*z* = 296 (30) [M^+], 265 (100), 237 (6), 205 (53), 178 (22), 165 (21), 151 (9), 133 (10), 117 (9), 105 (80), 89 (25), 77 (100), 59 (7). $C_{18}H_{16}O_4$ (296.10): calcd. C 72.96, H 5.44; found C 72.91, H 5.38.

Carbonylation of 4e: According to the general procedure, using 24.0 mg of PdI_2 (6.7×10^{-2} mmol), 111.0 mg of KI (0.67 mmol), 400 mg of **4e** (2.00 mmol) and a mixture of 5 mL MeCN and 0.8 mL of MeOH at *T* = 80 °C, *p*(CO) = 2.4 MPa, *p*(air) = 0.8 MPa for 48 h, gave 226 mg of (*E*)-**5e** (39%).

(*E*)-3-Methoxy-1-[(butyl)(methoxycarbonyl)methylene]-3-methyl-1,3-dihydroisobenzofuran [(*E*)-5e]: Pale yellow oil. IR (film): $\tilde{\nu}$ = 2956 cm^{-1} (s), 2870 (m), 1711 (s), 1614 (s), 1462 (m), 1189 (m), 1116 (m), 1040 (s), 894 (w), 766 (m). ^1H NMR ($CDCl_3$): δ = 8.58−8.55 (m, 1 H, 7-H), 7.49−7.42 (m, 2 H, aromatic), 7.37−7.32 (m, 1 H, aromatic), 3.83 (s, 3 H, CO_2CH_3), 2.94 (s, 3 H, OCH_3), 2.62−2.57 (m, 2 H, CH_2), 1.75 (s, 3 H, CH_3), 1.52−1.47 (m, 2 H, CH_2), 1.42−1.36 (m, 2 H, CH_2), 0.94 (t, *J* = 7.3 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 169.3, 160.2, 142.8, 132.2, 130.3, 129.6, 126.6, 121.6, 109.9, 107.4, 51.2, 50.4, 31.2, 27.9, 25.7, 22.4, 13.9 ppm. MS: *m*/*z* = 290 (5) [M^+], 275 (4), 259 (20), 247 (12), 229 (50), 215 (60), 201 (15), 183 (25), 171 (27), 161 (75), 129 (100), 115 (33), 103 (19), 91 (32), 77 (25), 59 (12). $C_{17}H_{22}O_4$ (290.15): calcd. C 70.32, H 7.64; found C 70.25, H 7.60.

Carbonylation of 4f: According to the general procedure, using 24.0 mg of PdI_2 (6.7×10^{-2} mmol), 111.0 mg of KI (0.67 mmol), 372 mg of **4f** (2.00 mmol) and a mixture of 5 mL MeCN and 0.4 mL of MeOH at *T* = 80 °C, *p*(CO) = 2.4 MPa, *p*(air) = 0.8 MPa for 48 h, gave 265 mg of **6f** (48%) and 22 mg of **9f** (5%).

3-Butyl-1-methoxy-4-(methoxycarbonyl)benzo[*c*]pyran (6f): Yellow oil. IR (film): $\tilde{\nu}$ = 2956 cm^{-1} (m), 2832 (w), 1715 (s), 1608 (w), 1220 (w), 1121 (m), 1084 (m), 1038 (s), 997 (m), 754 (w). ^1H NMR

($CDCl_3$): δ = 7.61 (br. d, *J* = 8.0 Hz, 1 H, aromatic), 7.36 (td, *J* = 7.0, 1.8 Hz, 1 H, aromatic), 7.26 (td, *J* = 7.4, 1.0 Hz, 1 H, aromatic), 7.21 (dd, *J* = 7.4, 1.7 Hz, 1 H, aromatic), 5.91 (s, 1 H, OCH), 3.86 (s, 3 H, CO_2CH_3), 3.56 (s, 3 H, OCH_3), 2.73−2.53 (m, 2 H, =C-CH_2), 1.73−1.63 (m, 2 H, CH_2), 1.48−1.35 (m, 2 H, CH_2), 0.95 (t, *J* = 7.3 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 167.7, 161.2, 129.3, 127.7, 126.5, 125.9, 125.5, 123.4, 107.4, 99.6, 55.5, 51.4, 32.7, 29.8, 22.3, 13.8 ppm. MS: *m*/*z* = 276 (22) [M^+], 245 (100), 233 (9), 215 (67), 202 (10), 174 (17), 171 (24), 161 (27), 143 (23), 129 (28), 115 (65), 103 (31), 89 (62), 59 (29), 57 (26). $C_{16}H_{20}O_4$ (276.14): calcd. C 69.55, H 7.30; found C 69.46, H 7.27.

Carbonylation of 4g: According to the general procedure, using 24.0 mg of PdI_2 (6.7×10^{-2} mmol), 111.0 mg of KI (0.67 mmol), 432 mg of **4g** (2.00 mmol) and a mixture of 5 mL MeCN and 0.4 mL of MeOH at *T* = 85 °C, *p*(CO) = 2.4 MPa, *p*(air) = 0.8 MPa for 24 h, gave 324 mg of (*Z*)-**5g** (53%).

(*Z*)-3-Methoxy-1-[(methoxycarbonyl)(trimethylsilanyl)methylene]-3-methyl-1,3-dihydroisobenzofuran [(*Z*)-5g]: Colourless solid, 75−77 °C. IR (KBr): $\tilde{\nu}$ = 2949 cm^{-1} (s), 2898 (s), 2832 (m), 1707 (s), 1623 (m), 1242 (m), 1034 (s), 843 (s), 760 (m). ^1H NMR ($CDCl_3$): δ = 7.71 (dd, *J* = 7.5, 1.1 Hz, 1 H, aromatic), 7.47−7.32 (m, 3 H, aromatic), 3.82 (s, 3 H, CO_2CH_3), 2.96 (s, 3 H, OCH_3), 1.73 (s, 3 H, CH_3), 0.27 [s, 9 H, $Si(CH_3)_3$] ppm. ^{13}C NMR ($CDCl_3$): δ = 171.2, 162.6, 142.0, 132.2, 130.5, 129.6, 124.1, 122.0, 110.5, 103.2, 51.5, 50.5, 25.5, −0.8 ppm. MS: *m*/*z* = 306 (3) [M^+], 291 (2), 275 (3), 259 (12), 187 (11), 171 (100), 115 (16), 89 (39), 73 (27), 59 (27). $C_{16}H_{22}O_4Si$ (306.13): calcd. C 62.71, H 7.24; found C 62.67, H 7.21.

Carbonylation of 4h: According to the general procedure, using 24.0 mg of PdI_2 (6.7×10^{-2} mmol), 111.0 mg of KI (0.67 mmol), 404 mg of **4h** (2.00 mmol) and 5.4 mL of MeOH at *T* = 105 °C, *p*(CO) = 2.4 MPa, *p*(air) = 0.8 MPa for 48 h, gave 23 mg of **6h** (4%) and 168 mg (36%) of **9h**. The same reaction carried out in a mixture of 5 mL MeCN and 0.4 mL of MeOH led to the product (*E*)-**5h** (64 mg, 11%).

(*E*)-3-Methoxy-1-[(methoxycarbonyl)(trimethylsilanyl)methylene]-1,3-dihydroisobenzofuran [(*E*)-5h]: Colourless oil. IR (film): $\tilde{\nu}$ = 2947 cm^{-1} (m), 2836 (w), 1704 (s), 1650 (s), 1465 (m), 1372 (m), 1247 (s), 1073 (s), 1039 (s), 957 (s), 842 (m), 766 (m). ^1H NMR ($CDCl_3$): δ = 7.70−7.67 (m, 1 H, 7-H), 7.44−7.38 (m, 3 H, aromatic), 6.31 (s, 1 H, OCH), 3.81 (s, 3 H, CO_2CH_3), 3.42 (s, 3 H, OCH_3), 0.27 [s, 9 H, $Si(CH_3)_3$] ppm. ^{13}C NMR ($CDCl_3$): δ = 167.6, 163.1, 139.5, 132.3, 130.3, 129.9, 124.0, 122.9, 105.4, 104.1, 54.3, 51.5, −0.7 ppm. MS: *m*/*z* = 292 (1) [M^+], 277 (2), 261 (2), 233 (10), 188 (10), 173 (10), 157 (100), 101 (16), 89 (40), 73 (20), 59 (24). $C_{15}H_{20}O_4Si$ (292.11): calcd. C 61.61, H 6.89; found C 61.49, H 6.87.

1-Methoxy-4-(methoxycarbonyl)-3-(trimethylsilanyl)benzo[*c*]pyran (6h): Colourless oil. IR (film): $\tilde{\nu}$ = 2952 cm^{-1} (m), 1714 (s), 1435 (w), 1324 (m), 1248 (m), 1208 (s), 1076 (s), 1043 (s), 935 (m), 840 (m), 756 (m). ^1H NMR ($CDCl_3$): δ = 7.96 (dd, *J* = 8.0, 1.0 Hz, 1 H, aromatic), 7.40 (ddd, *J* = 7.3, 7.9, 1.5 Hz, 1 H, aromatic), 7.31 (ddd, *J* = 7.3, 7.2, 1.0 Hz, 1 H, aromatic), 7.23 (dd, *J* = 7.5, 1.4 Hz, 1 H, aromatic), 5.92 (s, 1 H, OCH), 3.84 (s, 3 H, CO_2CH_3), 3.53 (s, 3 H, OCH_3), 0.29 [s, 9 H, $Si(CH_3)_3$] ppm. ^{13}C NMR ($CDCl_3$): δ = 169.8, 167.5, 129.3, 127.3, 126.6, 126.4, 125.4, 123.4, 118.7, 99.0, 55.6, 51.1, −1.1 ppm. MS: *m*/*z* = 292 (2) [M^+], 277 (18), 261 (6), 233 (7), 203 (7), 188 (19), 173 (13), 160 (20), 145 (26), 89 (54), 73 (100), 59 (31). $C_{15}H_{20}O_4Si$ (292.11): calcd. C 61.61, H 6.89; found C 61.52, H 6.86.

Carbonylation of 4i: According to the general procedure, using 24.0 mg of PdI_2 (6.7×10^{-2} mmol), 111.0 mg of KI (0.67 mmol), 412 mg of **4i** (2.00 mmol) and a mixture of 5 mL MeCN and 0.4 mL of MeOH at *T* = 80 °C, *p*(CO) = 2.4 MPa, *p*(air) = 0.8 MPa for 48 h, gave 136 mg of (*E*)-**5i** (23%), and 225 mg of (*Z*)-**5i** (38%).

(*E*)-3-Methoxy-1-[(methoxycarbonyl)methylene]-3-phenyl-1,3-dihydroisobenzofuran [(*E*)-5i]: Pale yellow oil. IR (film): $\tilde{\nu}$ = 3072 cm^{-1} (m), 2941 (m), 2833 (w), 1706 (s), 1636 (s), 1464 (m), 1374 (m), 1226 (m), 1113 (s), 956 (m), 765 (m). ^1H NMR ($CDCl_3$): δ = 9.18−9.15 (m, 1 H, aromatic), 7.57−7.50 (m, 4 H, aromatic), 7.38−7.30 (m, 4 H, aromatic), 5.91 (s, 1 H, =CH), 3.81 (s, 3 H, CO_2CH_3), 3.22 (s, 3 H, OCH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 167.8, 167.1, 143.7, 139.3, 131.9, 131.2, 130.0, 128.8, 128.3 (2), 128.0, 125.5 (2), 122.8, 111.6, 93.1, 51.2, 51.0 ppm. MS: *m*/*z* = 296 (21) [M^+], 281 (3), 265 (72), 237 (100), 233 (60), 219 (38), 205 (58), 193 (18), 178 (80), 165 (80), 152 (57), 117 (41), 105 (45), 77 (83), 59 (28). $C_{18}H_{16}O_4$ (296.10): calcd. C 72.96, H 5.44; found C 72.92, H 5.38.

(*Z*)-3-Methoxy-1-[(methoxycarbonyl)methylene]-3-phenyl-1,3-dihydroisobenzofuran [(*Z*)-5i]: Pale yellow oil. IR (film): $\tilde{\nu}$ = 3058 cm^{-1} (w), 2944 (m), 2935 (w), 1708 (s), 1657 (s), 1467 (m), 1274 (m), 1160 (s), 916 (m). ^1H NMR ($CDCl_3$): δ = 7.62−7.53 (m, 4 H, aromatic), 7.49−7.32 (m, 5 H, aromatic), 5.62 (s, 1 H, =CH), 3.79 (s, 3 H, CO_2CH_3), 3.27 (s, 3 H, OCH_3) ppm; the NOESY tp spectrum shows the presence of an interaction between a vinyl proton (δ = 5.62 ppm) and an aromatic proton (δ = 7.62−7.53 ppm). ^{13}C NMR ($CDCl_3$): δ = 166.0, 163.8, 142.0, 138.9, 133.3, 131.6, 130.0, 128.8, 128.4 (2), 125.7 (2), 123.3, 121.2, 114.7, 87.2, 51.6, 50.9 ppm. MS: *m*/*z* = 296 (20) [M^+], 265 (70), 237 (100), 233 (62), 219 (38), 205 (59), 193 (43), 178 (95), 165 (92), 152 (71), 117 (57), 105 (61), 77 (100), 59 (41). $C_{18}H_{16}O_4$ (296.10): calcd. C 72.96, H 5.44; found C 72.90, H 5.40.

Dimethyl 2-(2-Dimethoxymethylphenyl)-but-2-enedioate (9b): Colourless oil. IR (film): $\tilde{\nu}$ = 2952 cm^{-1} (w), 2848 (w), 1728 (s), 1435 (m), 1349 (m), 1281 (m), 1213 (s), 1088 (m), 765 (m). ^1H NMR ($CDCl_3$): δ = 7.69−7.66 (m, 2 H, aromatic), 7.36−7.34 (m, 2 H, aromatic), 6.12 (s, 1 H, OCH), 5.42 (s, 1 H, =CH), 3.83 (s, 3 H, CO_2CH_3), 3.81 (s, 3 H, CO_2CH_3), 3.33 (s, 6 H, OCH_3) ppm. MS: *m*/*z* = 294 (2) [M^+], 263 (13), 235 (100), 203 (75), 175 (27), 145 (50), 75 (40), 59 (14). $C_{15}H_{18}O_6$ (294.11): calcd. C 61.22, H 6.16; found C 61.17, H 6.14.

Acknowledgments

This work was supported by the Ministero dell'Università e della Ricerca Scientifica e Tecnologica (Progetto d'Interesse Nazionale PIN MM03027791).

[1] B. Gabriele, M. Costa, G. Salerno, G. P. Chiusoli, *J. Chem. Soc., Perkin Trans. 1* **1994**, 83−87.
[2] B. Gabriele, G. Salerno, M. Costa, G. P. Chiusoli, *J. Organomet. Chem.*, **2003**, *687*, 219−228.
[3] S. Berteina, A. De Mesmaeker, *Synlett* **1998**, 1227−1230.
[4] Fürstner, H. Szillat, F. Stelzer, *J. Am. Chem. Soc.* **2000**, *122*, 6785−6786.
[5] For a discussion on stereoelectronic effects on cyclisation reactions, see: E. E. Eliel, S. H. Wilen, L. N. Mander, *Stereochemistry of Organic Compounds*, Wiley-Interscience, New York, **1994**, pp. 684−685.
[6] P. G. Sammes, D. J. Weller, *Synthesis* **1995**, 1205−1222.
[7] N. Asao, T. Nogami, K. Takahashi, Y. Yamamoto, *J. Am. Chem. Soc.* **2002**, *124*, 764−765.

[8] Oxidative cyclization/carbonylation of 4-ynones, in the presence of $[PdCl_2(CH_3CN)_2]$ as catalyst and 1,4-benzoquinone as oxidizing agent, to give cyclic ketals or cyclic orthoester derivatives through the intermediate formation of the corresponding hemiketals has been reported recently: [8a] K. Kato, Y. Yamamoto, H. Akita, *Tetrahedron Lett.* **2002**, *43*, 4915−4917. [8b] K. Kato, Y. Yamamoto, H. Akita, *Tetrahedron Lett.* **2002**, *43*, 6587−6590.

[9] Dihydroisobenzofurans have found application as synthetic intermediates for the synthesis of biologically active compounds. See, for example: D. S. Brown, M. C. Elliott, C. J. Moody, T. J. Mowlem, *J. Chem. Soc., Perkin Trans. 1* **1995**, 1137−1144.

[10] Some benzo[*c*]pyran derivatives have shown interesting pharmacological activity. See, for example: [10a] M. R. Michaelides, R. Schoenleber, S. Thomas, D. M. Yamamoto, D. R. Britton, R. MacKenzie, J. W. Kebabian, *J. Med. Chem.* **1991**, *34*, 2946−2953. [10b] M. P. DeNinno, R. Schoenleber, R. J. Perner, L. Lijewski, K. E. Asin, D. R. Britton, R. MacKenzie, J. W. Kebabian, *J. Med. Chem.* **1991**, *34*, 2561−2569.

[11] B. Gabriele, G. Salerno, A. Fazio, R. Pittelli, *Tetrahedron* **2003**, *59*, 6251−6259.

[12] [12a] M. Katsuya, I. Nobuharu, *J. Am. Chem. Soc.* **1998**, *120*, 1928−1929. [12b] W. B. Austin, N. Bilow, W. J. Kellenghan, K. S. Y. Lau, *J. Org. Chem.* **1981**, *46*, 2280−2286. [12c] S. W. Zhang, T. Sugioka, S. Takahashi, *J. Mol. Catal. A., Chem.* **1999**, *143*, 211−218. [12d] K. R. Roesch, R. C. Larock, *J. Org. Chem.* **2002**, *67*, 86−94. [12e] G. Dyker, W. Stirner, G. Henkel, *Eur. J. Org. Chem.* **2000**, 1433−1441. [12f] J. W. Herndon, Y. Zhang, *J. Organomet. Chem.* **2001**, *634*, 1−4. [12g] M. Shindo, Y. Sato, K. Shishido, *J. Org. Chem.* **2001**, *63*, 7818−7824.

Received September 15, 2003

