



Highly substituted furans from 2-propynyl-1,3-dicarbonyls and organic halides or triflates via the oxypalladation-reductive elimination domino reaction

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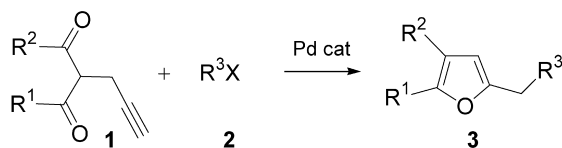
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Abstract—The palladium-catalysed reaction of 2-propynyl-1,3-dicarbonyls with organic halides or triflates provides an efficient straightforward entry into highly substituted furans. The best results have been obtained by using an excess of the alkyne. The process can tolerate a wide variety of important functional groups both on the alkyne and the organic halide or triflate. Under an atmosphere of carbon monoxide, the reaction affords furan derivatives incorporating carbon monoxide. Depending on the alkyne to organic halide or triflate ratio, acyl furans (incorporating one molecule of carbon monoxide) or enol esters (incorporating two molecules of carbon monoxide) can be isolated as the main products. © 2003 Elsevier Science Ltd. All rights reserved.

1. Introduction

The palladium-catalysed reaction of organic halides or triflates with alkynes containing carbon,¹ oxygen² and nitrogen³ nucleophiles close to the carbon–carbon triple bond has emerged as one of the most powerful and versatile tools for the synthesis of a variety of carbo- and heterocycles. During our studies on the extension of this chemistry to the construction of the furan ring, a common unit of numerous biologically active compounds,⁴ we observed and previously communicated⁵ that 2-propynyl-1,3-dicarbonyl compounds can be used as useful building blocks for the preparation of 2,3,5-trisubstituted furans (Scheme 1).

Now, we wish to report full details on this synthesis of highly functionalized furans.



Scheme 1.

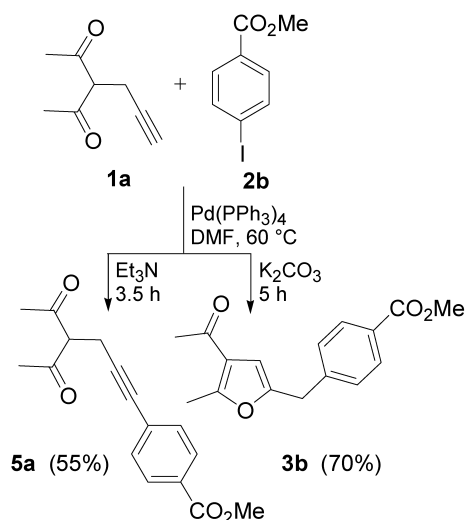
Keywords: alkynes; palladium; cyclization; catalysis.

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2. Results and discussion

Starting 2-propynyl-1,3-dicarbonyls **1** were readily prepared by alkylation of 1,3-dicarbonyl compounds with propargyl bromide in the presence of DBU in toluene.⁶ Initial cyclization attempts were focused on finding a general set of reaction conditions that could be used with a wide variety of 2-propynyl-1,3-dicarbonyls and organic halides or triflates. The influence of the base, the catalyst system and the 1:2 molar ratio on the reaction outcome was examined. The nature of the base was found to play a pivotal role in controlling the cyclization–coupling balance.⁷ As an example, the reaction of **1a** with methyl *p*-iodobenzoate gave the furan derivative **3b** as the main product in the presence of potassium carbonate and the coupling derivative **5a** as the main product by using Et₃N (Scheme 2).

Apparently, with K₂CO₃ the intramolecular nucleophilic attack of the oxygen across the carbon–carbon triple bond co-ordinated to palladium is favoured (*vide infra*), whereas in the presence of the amine co-ordination of the carbon–carbon triple bond to palladium results in the activation of the terminal hydrogen atom towards basic attack. Formation of the carbon–palladium bond between the incipient acetylide anion and palladium generates a σ -alkynyl- σ -organopalladium complex⁸ that subsequently affords the coupling product **5** by a reductive elimination step. Pd(PPh₃)₄ was more effective than other commonly used palladium catalysts (Table 1). As for the 1:2 molar ratio, we started our study using an excess of the aryl halide (procedure A). However, better results were possible when



Scheme 2.

an excess of the alkyne was employed, typically 1.5 equiv. (Table 1, entry 5).

Subsequently, the following reaction conditions were employed when we explored the scope and limitations of this route to highly functionalized furans by examining a variety of 2-propynyl-1,3-dicarbonyls, aryl halides and vinyl triflates: (procedure B) **1** (1.5 equiv.), **2** (1 equiv.), K_2CO_3 (5 equiv.), $\text{Pd}(\text{PPh}_3)_4$ (0.05 equiv.). Under these conditions, a wide range of substituted furan derivatives have been prepared in good yield (Table 2). The reaction tolerates a variety of functionalized aryl bromides and vinyl triflates. Several 2-propynyl-1,3-dicarbonyl compounds have also been employed successfully. As for the latter, **1d,g** represent the only exceptions among the 2-propynyl-1,3-dicarbonyls that we have explored. Compound **1d** was recovered almost unchanged after treatment with **2l** under our standard cyclization conditions. Increase of the reaction temperature to 120°C resulted in the formation of a mixture of the isomeric furans **3n,n'** (Table 2, entry 18). Compound **1g**, containing aryl and alkyl ketone fragments, gave rise to a mixture of furan products even at 60°C , although with a prevalence of the furan derived from the cyclization involving the oxygen of the alkyl ketone fragment (Table 2, entries 20 and 21).

Internal alkynes can also be used in this chemistry to give

Table 1. Catalyst system and **1a:2a** ratio in the synthesis of **3b**

Entry	Catalyst system	1a:2a	Yield % of 3b ^a
1	$\text{Pd}_2(\text{dba})_3$	1:2	30
2	$\text{Pd}(\text{dppe})_2$ ^b	1:2	40
3	$\text{Pd}(\text{OAc})_2/\text{P}(o\text{-tol})_3$ ^c	1:2	40
4	$\text{Pd}(\text{PPh}_3)_4$	1:2	52
5	$\text{Pd}(\text{PPh}_3)_4$	1.5:1.0	93

Reactions were carried out in DMF, at 60°C , in the presence of 5 equiv. of K_2CO_3 and 0.05 equiv. of [Pd] under a nitrogen atmosphere.

^a Yields are given for isolated products.

^b $\text{dppe}=[1,2\text{-bis}(\text{diphenylphosphino})\text{ethane}]$.

^c 0.1 equiv. of $\text{P}(o\text{-tol})_3$.

furan derivatives containing branched side chains (Scheme 3).

Compounds **5a–b** could be prepared through the palladium-catalysed reaction of **1a,c** with aryl halides in the presence of Et_3N (Scheme 2). However, better results were obtained in the presence of added CuI as co-catalyst.⁹ Particularly, the highest yields were obtained by using PdCl_2 , dppf [1,1'-bis(diphenylphosphino)ferrocene], and CuI in the presence of Et_3N ¹⁰ (Table 3, entries 7 and 8). Depending on the reaction conditions, competitive cyclization of **1a** to 2,5-dimethyl-3-acetylfuran can be observed (Table 3, entry 2). As shown by the results shown in Table 3 (entries 3 and 4), both palladium and copper¹¹ can catalyse this cyclization. The base-promoted cyclization mechanism appears unlikely on the basis of the fact that no cyclization product was observed upon treatment of **1a** with K_2CO_3 or amine bases.

As for the reaction mechanism, most probably 2,3,5-trisubstituted furans **3** are generated through the oxypalladation–reductive elimination domino mechanism² which involves: (a) coordination of the organopalladium complex formed in situ to the acetylenic system, (b) intramolecular nucleophilic attack of the oxygen across the activated carbon–carbon triple bond to give oxypalladation adducts, (c) reductive elimination of $\text{Pd}(0)$ species (Scheme 4).

Isolation of the deuterio derivative **8** (47%) upon treatment of 6-deuterio-3-acetyl-5-hexyn-2-one **7** with methyl *p*-iodobenzoate under usual conditions (Scheme 5) rules out the possible formation of the furan ring through a mechanism involving cleavage of the $\text{C}_{\text{sp}}\text{–H}$ bond.

Further support for the oxypalladation–reductive elimination mechanism is given by the *E* stereochemistry of the alkyldiene derivative **4a** obtained from the reaction of **1c** with *p*-nitroiodobenzene (Table 2, entry 15). Interestingly, the formation of alkyldiene intermediates is usually observed in the related palladium-catalysed reaction of 3-oxo-6-heptynoates with aryl halides,¹² but **4a** is the only example of a compound of this type isolated in the oxypalladation–reductive elimination of 2-propynyl-1,3-dicarbonyls.

We next investigated the palladium-catalysed reaction of 2-propynyl-1,3-dicarbonyls with organic halides or triflates in the presence of carbon monoxide with the aim of preparing substituted furans incorporating a molecule of carbon monoxide.¹³ Our task was to develop a simple three component route to acyl derivatives **9** (Scheme 6).

Since our related study on the carbonylative aminopalladation–reductive elimination of *o*-alkynyltrifluoroacetanilides with organic halides showed that reactions with electron-poor aryl halides are likely to prove the most difficult,¹⁴ we turned our attention to optimising the reaction of **1a** with *p*-chlorophenyl iodide **2a**.


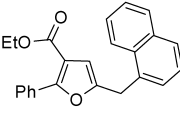
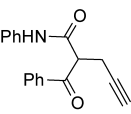
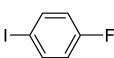
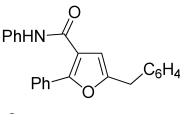
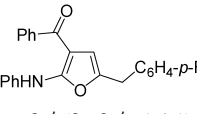
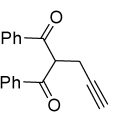
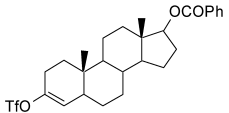
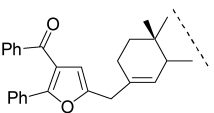
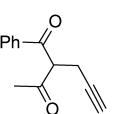

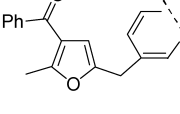
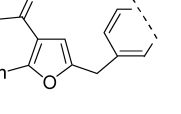
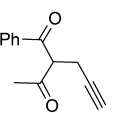
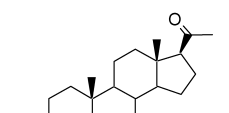
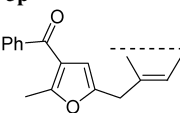
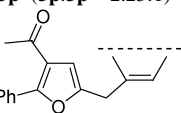
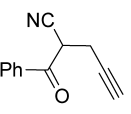
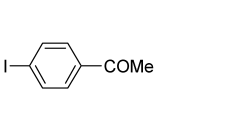
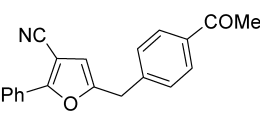
The reaction was carried out under a balloon of carbon monoxide. The nature of the catalyst system, the reaction temperature and the **1a:2a** molar ratio were found to influence the course of the reaction. The best results were obtained at 60°C by use of a **1a:2a** 1.5:1 molar ratio in the

Table 2. Palladium-catalysed synthesis of 2,3,5-trisubstituted furans **3** from 2-propynyl-1,3-dicarbonyl compounds **1** and organic halides or triflates **2**

Entry	Alkyne 1	Organic halide or triflate 2	Procedure	<i>t</i> (h)	Product 3	Yield % ^a	
1			2a	A	1.5		3a 52
2			2a	B	4		3a 93
3			2b	A	1.5		3b 56
4			2b	B	5		3b 70
5			2c	A ^b	3		3c 62
6			2c	B ^b	3		3c 98
7			2d	B	6		3d 67
8			2e	B	1.5		3e 66
9			2f	B	2.5		3f 67
10			2g	B	2.5		3g 71
11			2h	B	2.5		3h 56
12			2i	B	7		3i 66
13			2g	B	3.5		3j 55
14			2a	B	3		3k 93
15			2j	B	5		4a 74
16			2g	B	24		3l 31

(continued on next page)

Table 2 (continued)

Entry	Alkyne 1	Organic halide or triflate 2	Procedure	<i>t</i> (h)	Product 3	Yield % ^a	
17	1c		2k B	6		3m 35	
18			2l B ^c		 + 	3n 3n' (3n:3n' =1.4:1)	83
19			2m B	1.5		3o	60
20			2g B	2	 + 	3p 3p' (3p:3p' =2.25:1)	78
21			2n B	4	 + 	3q 3q' (3q:3q' =3.12:1)	79
22			2o B	5		3r	66

Unless otherwise stated, reactions were carried out at 60°C in DMF, under a nitrogen atmosphere, using (procedure A) 1 equiv. of **1**, 2 equiv. of **2**, 5 equiv. of K₂CO₃, and 0.05 equiv. of Pd(PPh₃)₄ or (procedure B) 1.5 equiv. of **1**, 1 equiv. of **2**, 5 equiv. of K₂CO₃, and 0.05 equiv. of Pd(PPh₃)₄.

^a Yields are given for isolated products.

^b 90°C.

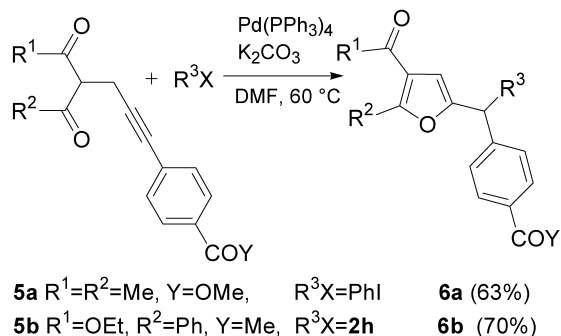
^c 120°C.

presence of Pd(OAc)₂ and P(*o*-tol)₃ (Table 4, entry 10). The catalyst system was prepared in situ from 1 equiv. of Pd(OAc)₂ and 4 equiv. of P(*o*-tol)₃. We have not investigated the effect of the Pd/P ratio on the course of the reaction. Both Pd(OAc)₂ (Table 4, entry 2) and PdCl₂(PhCN)₂ (Table 4, entry 3) were found to be effective catalysts. However, precipitation of palladium was occasionally observed, precluding reproducibility. Use of phosphine ligands such as PPh₃, P(*p*-tol)₃, dppf, and dppe resulted in the formation of significant amounts of **3a**,

derived from the noncarbonylative cyclization of **1a**. An excess of **2a** was found to favour the formation of the enol ester **10a** and with the Pd(OAc)₂/P(*o*-tol)₃ catalyst system at 60°C, **10a** was isolated in 51% yield (Table 4, entry 7).

Using the best conditions found for the formation of **9a** [(procedure C) **1** (1.5 equiv.), **2** (1 equiv.), Pd(OAc)₂ (0.05 equiv.), P(*o*-tol)₃ (0.20 equiv.), K₂CO₃ (5 equiv.) in MeCN at 60°C under a balloon of carbon monoxide], a variety of furan derivatives **9** have been prepared in good yield. Our preparative results are summarized in Table 5 (entries 1, 3, 5–8, 10, 12).

Application of these conditions to vinyl triflates, however, met with failure. For example, no evidence of the corresponding furan derivative was attained when **1b** was treated with naphthyl triflate **2g** (Table 6, entry 1). After some experimentation (Table 6, entries 2–11), we were pleased to find that acyl furans containing a vinyl fragment could be formed in satisfactory yield by using the following conditions: (procedure D) **1** (1.5 equiv.), **2** (1 equiv.), Pd(PPh₃)₄ (0.05 equiv.), K₂CO₃ (5 equiv.) in MeCN at 60°C under 2 atm of carbon monoxide. Our preparative results are listed in Table 5 (entries 14, 15, 17, 18).



Scheme 3.

Table 3. Palladium–copper catalysed synthesis of **5** from 2-propynyl-1,3-dicarbonyls and aryl halides

Entry	Alkyne 1	Aryl halide 2	<i>T</i> (°C)/ <i>t</i> (h)	1:2	Catalytic system	Base	Yield % ^a		
							5	2,5-dimethyl-3-acetylfuran	3
1 ^b	1a	2b	60/3.5	1:2	Pd(PPh ₃) ₄	Et ₃ N	55 (5a)	–	–
2 ^{c,d}	1a	2b	rt/12	1:1	Pd(PPh ₃) ₄ , CuI	Et ₂ NH	41 (5a)	30	–
3 ^e	1a	2b	rt/12	1:1	Pd(PPh ₃) ₄	Et ₂ NH	–	80	–
4 ^f	1a	2b	rt/12	1:1	CuI	Et ₂ NH	–	50	–
5 ^g	1a	2b	60/4	1.2:1	PdCl ₂ , dppf, CuI	Et ₃ N	34 (5a)	–	35 (3b)
6 ^g	1a	2b	60/5	1.2:1	PdCl ₂ , tcpp, ^h CuI	Et ₃ N	40 (5a)	–	18 (3b)
7 ^g	1a	2b	30/24	1.2:1	PdCl ₂ , dppf, CuI	Et ₃ N	85 (5a)	–	–
8 ^g	1c	2o	30/24	1.2:1	PdCl ₂ , dppf, CuI	Et ₃ N	94 (5b)	–	–

All the reactions were carried out in DMF.

^a Yields are given for isolated products.

^b **1a:2b**:Pd(PPh₃)₄:Et₃N=1:2:0.02:5.

^c **1a:2b**:Pd(PPh₃)₄:CuI:Et₂NH=1:0.02:20.

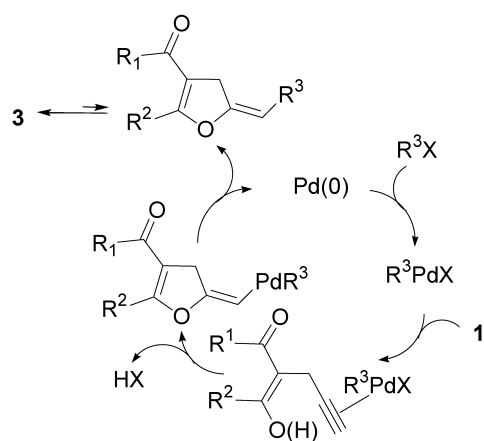
^d Methyl 4-iodobenzoate was recovered in 36% yield.

^e **1a**:Pd(PPh₃)₄:Et₃N=1:2:0.02:5.

^f **1a**:CuI:Et₂NH=1:0.01:20.

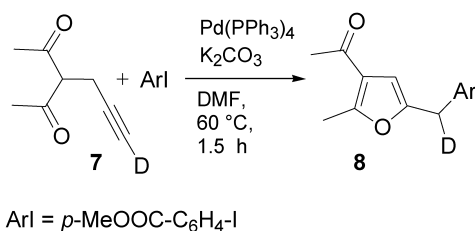
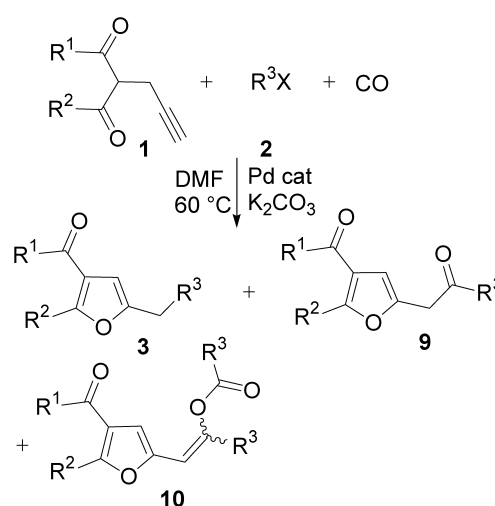
^g **1:2**:PdCl₂:ligand:CuI:Et₃N=1.2:1:0.04:0.04:0.02:5.

^h tcpp=tris(*p*-chlorophenyl)phosphine.

**Scheme 4.**

Enol esters **10** have been prepared in satisfactory yield by use of the following conditions: (procedure E) **1** (1 equiv.), **2** (3 equiv.), Pd(OAc)₂ (0.05 equiv.), P(*o*-tol)₃ (0.2 equiv.), K₂CO₃ (5 equiv.) in DMF at 60°C under a balloon of carbon monoxide (Table 5, entries 2, 4, 9, 11, 13). Compound **10** were obtained exclusively or predominantly as *E* isomers. Their stereochemistry was assigned by NMR analysis.¹⁵ Vinyl protons in the *E* isomers are downfield from vinyl protons in the *Z* isomers.

We believe that the formation of acylfurans **9** proceeds through a mechanism similar to that proposed by us for the related synthesis of 3-acylindoles from *o*-alkynyltrifluoroacetanilides¹⁴ and that ultimately involves: (a) coordination of the alkyne to an acylpalladium complex, (b) intramolecular

**Scheme 5.****Scheme 6.****Table 4.** Palladium-catalysed reaction of **1a** with *p*-chloriodobenzene in MeCN under a balloon of carbon monoxide

Entry	Catalyst system (Pd–ligand ratio)	<i>T</i> (°C)	1a:2a	Yield % ^a		
				3a	9a	10a
1	Pd(PPh ₃) ₄	45	0.8	23	19	–
2	Pd(OAc) ₂	45	0.8	2	54	–
3	PdCl ₂ (PhCN) ₂	60	1.5	–	69	–
4	Pd(dba) ₂ /P(<i>o</i> -tol) ₃ (1:4)	45	0.8	–	22	–
5	Pd(OAc) ₂ /P(<i>o</i> -tol) ₃ (1:4)	45	0.8	–	33	–
6	Pd(OAc) ₂ /P(<i>o</i> -tol) ₃ (1:4)	25	0.8	–	Traces	–
7	Pd(OAc) ₂ /P(<i>o</i> -tol) ₃ (1:4)	60	0.5	–	–	51
8	Pd(OAc) ₂ /P(<i>o</i> -tol) ₃ (1:4)	45	0.5	–	12	34
9	Pd(OAc) ₂ /P(<i>o</i> -tol) ₃ (1:4)	60	0.8	–	30	19
10	Pd(OAc) ₂ /P(<i>o</i> -tol) ₃ (1:4)	60	1.5	–	64	–
11	Pd(OAc) ₂ /P(<i>p</i> -tol) ₃ (1:4)	60	1.5	20	17	–
12	Pd(OAc) ₂ /dppf (1:2)	60	1.5	21	18	–
13	Pd(OAc) ₂ /dppp ^b (1:2)	60	1.5	–	33	–
14	Pd(dppe) ₂	60	1.5	23	47	–

Reactions were carried out at 60°C overnight in anhydrous MeCN under a balloon of carbon monoxide using 1 equiv. of **1a**, 5 equiv. of K₂CO₃, and 0.05 equiv. of [Pd].

^a Yields are given for isolated products.

^b dppp=1,3-bis(diphenylphosphino)propane.

Table 5. Palladium-catalysed synthesis of furans **9** and **10**

Entry	Alkyne 1	Organic halide or triflate 2	Procedure	Yield % ^a	
				9	10
1	1a	2a	C	64 (9a)	–
2	1a	2a	E	–	51 (10a)
3	1a	<i>m</i> -F–C ₆ H ₄ –I 2p	C	55 (9b)	–
4	1a	2p	E	–	54 (10b) ^b
5	1a	2b	C	33 (9c) ^c	–
6	1a	2b ^d	C	53 (9c) ^c	–
7	1a	2b	C	41 (9c) ^f	–
8	1a	2b ^{f,g}	C	45 (9c)	–
9	1a	2b	E	–	54 (10c)
10	1a	PhI 2q	C	60 (9d)	–
11	1a	2q	E	–	58 (10d) ^h
12	1a	<i>m</i> -Me–C ₆ H ₄ –I 2r	C	60 (9e)	–
13	1a	2r	E	–	57 (10e) ⁱ
14	1b	2g	D	62 (9f)	–
15	1b	2m	D	62 (9g)	–
16	1a	2d	C	–	–
17	1a	2d	D	50 (9h)	–
18	1a	2h	D	57 (9i)	–

Unless otherwise stated, reactions were carried out at 60°C overnight, in anhydrous acetonitrile, under an atmosphere of carbon monoxide, using: (procedure C, balloon of carbon monoxide) 1.5 equiv. of **1**, 1 equiv. of **2**, 5 equiv. of K₂CO₃, 0.05 equiv. of Pd(OAc)₂ and 0.20 equiv. of P(*o*-tol)₃; (procedure D, pCO=2 atm) 1.5 equiv. of **1**, 1 equiv. of **2**, 5 equiv. of K₂CO₃, 0.05 equiv. of Pd(PPh₃)₄; (procedure E, balloon of carbon monoxide) 1 equiv. of **1**, 2 equiv. of **2**, 5 equiv. of K₂CO₃, and 0.05 equiv. of Pd(OAc)₂ and 0.20 equiv. of P(*o*-tol)₃.

^a Yields are given for isolated products.

^b *E*:*Z*=90:10 (NMR analysis). Further purification gave the pure *E* isomer in 45% yield.

^c Compound **3b** was isolated in 21% yield.

^d 1.5 atm of carbon monoxide.

^e Compound **3b** was isolated in 15% yield.

^f 2 atm of carbon monoxide.

^g **1a**:**2b**=2:1.

^h *E*:*Z*=77:23 (NMR analysis). Further purification gave the pure *E* isomer in 40% yield.

ⁱ *E*:*Z*=68:32 (NMR analysis). Further purification gave the pure *E* isomer in 37% yield.

nucleophilic attack of the oxygen across the activated carbon–carbon triple bond to give oxypalladation adducts, (c) reductive elimination of Pd(0) species, (d) isomerization of the resultant alkylidene derivative.

As for the enol esters, presumably they are generated through acylation of enolates **12** (formed from the acylfurans **9**) as shown in Scheme 7.

In summary, easily available 2-propynyl-1,3-dicarbonyl and

Table 6. Palladium-catalysed reaction of **1b** with naphthyl triflate **2g** in the presence of carbon monoxide

Entry	Catalyst system (Pd:ligand ratio)	ⁿ Bu ₄ NCl (1 equiv.)	Time (h)	Yield % ^a	
				3j	9f
1	Pd(OAc) ₂ /P(<i>o</i> -tol) ₃ (1:4)	–	–	–	–
2	Pd(OAc) ₂ /P(<i>o</i> -tol) ₃ (1:4)	+	21	–	–
3	PdCl ₂ (PhCN) ₂	–	–	–	–
4	Pd ₂ (dba) ₃	–	–	–	–
5	Pd(dppe) ₂	–	57	11	–
6	Pd(dppe) ₂	–	73	11	–
7	Pd(PPh ₃) ₄	–	15	42	–
10 ^b	Pd(PPh ₃) ₄	+	53	20	–
11 ^{c,d}	Pd(PPh ₃) ₄	–	–	–	62

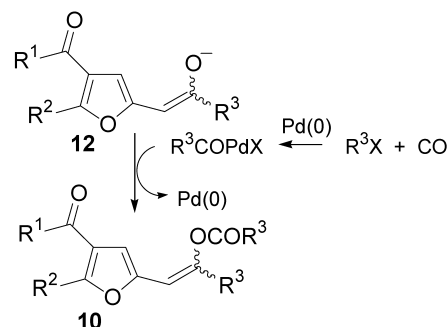
Unless otherwise stated, reactions were carried out in MeCN overnight, at 60°C, under a balloon of carbon monoxide using 1.5 equiv. of **1b**, 1 equiv. of **2g**, 5 equiv. of K₂CO₃, and 0.05 equiv. of [Pd].

^a Yields are given for isolated products.

^b 2,5-Dimethyl-3-acetylfuran was isolated in 10% yield.

^c 2 atm of carbon monoxide.

^d 2,5-Dimethyl-3-acetylfuran was isolated in 5% yield.

**Scheme 7.**

2-propynyl-1-cyano-3-carbonyl derivatives may represent useful building blocks for the preparation of highly substituted furans through oxypalladation–reductive elimination domino reactions. Employing K₂CO₃ instead of amine bases tends to favour the oxypalladation–reductive elimination mechanism over the coupling process. With internal alkynes, furan derivatives containing branched side chains can be prepared. In the presence of carbon monoxide, and depending on reaction conditions, the reaction can produce 1,2,5-trisubstituted furans incorporating one or two molecules of carbon monoxide.

3. Experimental

3.1. General

Melting points were uncorrected and were measured with a

Büchi apparatus. ^1H NMR (200 MHz) and ^{13}C NMR (50.3 MHz) spectra (CDCl_3 , unless otherwise stated; TMS as internal standard) were recorded with a Bruker AC 200 E spectrometer. EI (70 eV) mass spectra were recorded with a Saturn 2100T GC/MS Varian instrument and a TSQ 700 Finnigan/Mat instrument. IR spectra (KBr, unless otherwise stated) were recorded with a Perkin–Elmer 683 spectrometer. Only the most significant IR absorptions are given. Unless otherwise stated, all starting materials, catalysts, ligands, bases, and solvents are commercially available and were used as purchased, without further purification. Vinyl triflates were prepared according to Ref. 16. 2-Propynyl-1,3-dicarbonyl derivatives **1a–h** were prepared according to Ref. 6. Reaction products were purified by flash chromatography on silica gel eluting with *n*-hexane/EtOAc mixtures.

3.1.1. Synthesis of 2,3,5-trisubstituted furans 3a–r (procedure B). A typical procedure is as follows: to a solution of **1a** (0.189 g, 1.37 mmol) in DMF (4 mL), 1-chloro-4-iodobenzene **2a** (0.217 g, 0.91 mmol), potassium carbonate (0.630 g, 4.56 mmol), and $\text{Pd}(\text{PPh}_3)_4$ (0.045 g, 0.052 mmol) were added. The reaction mixture was gently purged with nitrogen and stirred at 60°C under a nitrogen atmosphere. After 4 h, ethyl acetate and 0.1N HCl were added; the organic layer was separated, washed with water, dried (Na_2SO_4) and the solvent evaporated in vacuo. The residue was purified by flash chromatography (95/5 *n*-hexane/EtOAc) to give **3a**.

Compound 3a. 0.21 g, 93% yield; mp $94\text{--}96^\circ\text{C}$. [Found: C, 67.4; H, 5.3. $\text{C}_{14}\text{H}_{13}\text{ClO}_2$ requires C, 67.61; H, 5.27]; ν_{max} 1660, 655, 610 cm^{-1} ; δ_{H} 2.32 (s, 3H, furanyl- CH_3), 2.51 (s, 3H, COCH_3), 3.85 (s, 2H, Ar- CH_2), 6.21 (s, 1H, furanyl- H), 7.15 (dd, $J=8.5, 4.3$ Hz, 2H, Ar- H), 7.25 (dd, $J=8.5, 4.3$ Hz, 2H, Ar- H); δ_{C} 14.3, 29.0, 33.4, 107.0, 122.1, 128.7, 130.0, 132.5, 135.8, 151.8, 157.6, 194.0; MS; m/z (relative intensity): 249 [(M+1) $^+$, 100], 234 (57).

Compound 3b. 70% yield; mp $69\text{--}70^\circ\text{C}$; lit. mp $69\text{--}70^\circ\text{C}$ and data consistent with that reported in the literature.⁵

Compound 3c. 98% yield; mp $116\text{--}118^\circ\text{C}$. [Found: C, 66.8; H, 5.6; N, 12.8. $\text{C}_{12}\text{H}_{12}\text{N}_2\text{O}_2$ requires C, 66.65; H, 5.59; N, 12.96]; ν_{max} 1720, 710, 620 cm^{-1} ; δ_{H} 2.37 (s, 3H, furanyl- CH_3), 2.54 (s, 3H, COCH_3), 3.98 (s, 2H, Ar- CH_2), 6.35 (s, 1H, furanyl- H), 8.88 (s, 2H, Ar- H), 9.14 (s, 1H, Ar- H); δ_{C} 14.3, 28.8, 29.1, 107.7, 122.2, 128.3, 131.9, 148.5, 156.9, 157.4, 158.1, 193.7; MS; m/z (relative intensity): 217 [(M+1) $^+$, 100], 201 (30).

Compound 3d. 67% yield; mp $103\text{--}104^\circ\text{C}$. [Found: C, 83.1; H, 10.4. $\text{C}_{35}\text{H}_{52}\text{O}_2$ requires C, 83.28; H, 10.38]; ν_{max} 1700, 1620, 620 cm^{-1} ; δ_{H} 0.70–1.42 (m, 41H, steroidal- H), 2.38 (s, 3H, furanyl- CH_3), 2.53 (s, 3H, COCH_3), 3.26 (s, 2H, $=\text{C}-\text{CH}_2$), 5.40 (bs, 1H, $=\text{C}-\text{H}$), 5.77 (s, 1H, $=\text{C}-\text{H}$), 6.23 (s, 1H, furanyl- H); δ_{C} 11.0, 12.4, 18.7, 18.9, 21.1, 22.5, 23.7, 23.8, 28.0, 28.2, 30.3, 31.8, 34.0, 35.8, 36.1, 38.7, 39.5, 39.7, 42.4, 46.2, 56.1, 56.9, 68.1, 106.6, 123.0, 126.4, 128.7, 132.0, 141.4, 151.8, 157.2, 194.4; MS; m/z (relative intensity): 504 (M^+ , 100).

Compound 3e. 66% yield; mp $102\text{--}104$. [Found: C, 76.8; H,

6.7. $\text{C}_{19}\text{H}_{20}\text{O}_3$ requires C, 77.00; H, 6.80]; ν_{max} 1660, 1590, 655, 615 cm^{-1} ; δ_{H} 2.23–2.29 (m, 2H, $-\text{CH}_2-\text{CH}_2-\text{CH}=\text{C}$), 2.32 (s, 3H, furanyl- CH_3), 2.51 (s, 3H, COCH_3), 2.76 (t, $J=7.8$ Hz, 2H, CH_2CH_2), 3.67 (s, 2H, $=\text{C}-\text{CH}_2$), 3.77 (s, 3H, $-\text{OCH}_3$), 5.76 (t, $J=4.5$ Hz, 1H, $=\text{C}-\text{H}$), 6.21 (s, 1H, furanyl- H), 6.65–6.65 (m, 2H, Ar- H), 7.10–7.14 (m, 1H, Ar- H); δ_{C} 11.0, 14.5, 23.1, 28.6, 29.1, 31.7, 55.1, 108.8, 110.8, 122.2, 123.8, 125.2, 127.3, 131.9, 138.3, 152.0, 157.1, 158.5, 194.2; MS; m/z (relative intensity): 297 [(M+1) $^+$, 100], 296 (M^+ , 67), 160 (84).

Compound 3f. 67% yield; oil. [Found: C, 79.9; H, 5.8. $\text{C}_{23}\text{H}_{20}\text{O}_3$ requires C, 80.21; H, 5.85]; ν_{max} (neat) 1680, 1600, 710, 660 cm^{-1} ; δ_{H} 2.35 (s, 3H, furanyl- CH_3), 2.54 (s, 3H, COCH_3), 3.57 (s, 2H, $=\text{C}-\text{CH}_2$), 5.62 (d, $J=2.4$ Hz, 1H, $-\text{OCH}$), 5.86 (d, $J=2.4$ Hz, 1H, $=\text{C}-\text{H}$), 6.30 (s, 1H, furanyl- H), 7.10–7.44 (m, 9H, Ar- H); δ_{C} 14.3, 29.1, 30.3, 76.6, 107.5, 110.1, 116.3, 118.0, 121.3, 123.4, 126.2, 126.5, 126.9, 128.2, 128.6, 129.6, 140.6, 150.3, 153.3, 157.3, 194.0; MS; m/z (relative intensity): 345 [(M+1) $^+$, 100], 344 (M^+ , 24).

Compound 3g. 71% yield; mp $51\text{--}52^\circ\text{C}$. [Found: C, 81.7; H, 6.0. $\text{C}_{18}\text{H}_{16}\text{O}_2$ requires C, 81.79; H, 6.10]; ν_{max} 1660, 620 cm^{-1} ; δ_{H} 2.29 (s, 3H, furanyl- CH_3), 2.51 (s, 3H, COCH_3), 4.01 (s, 2H, Ar- CH_2), 6.18 (s, 1H, furanyl- H), 7.30–7.44 (m, 3H, Ar- H), 7.63–7.80 (m, 4H, Ar- H); δ_{C} 14.3, 29.0, 34.3, 106.9, 122.1, 125.5, 126.1, 127.0, 127.1, 127.5, 127.6, 128.2, 132.3, 133.5, 134.7, 152.3, 157.5, 194.1; MS; m/z (relative intensity): 264 (M^+ , 100), 222 (11).

Compound 3h. 56% yield; mp $132\text{--}135^\circ\text{C}$. [Found: C, 76.5; H, 8.4. $\text{C}_{27}\text{H}_{34}\text{O}_3$ requires C, 79.76; H, 8.43]; ν_{max} 1740, 1680 cm^{-1} ; δ_{H} 0.91 (s, 3H, steroidal- CH_3), 0.95 (s, 3H, steroidal- CH_3), 1.00–2.30 (m, 15H, steroidal- H), 2.37 (s, 3H, furanyl- CH_3), 2.54 (s, 3H, COCH_3), 3.28 (s, 2H, $=\text{C}-\text{CH}_2$), 4.92 (bs, 1H, $=\text{C}-\text{H}$), 5.23 (s, 1H, $=\text{C}-\text{H}$), 6.25 (s, 1H, furanyl- H); δ_{C} 13.7, 14.4, 18.9, 20.4, 21.8, 25.9, 29.7, 30.6, 31.4, 34.9, 35.7, 35.8, 47.4, 48.4, 51.9, 106.6, 121.9, 122.1, 126.1, 132.5, 141.5, 151.7, 157.3, 194.3, 221.1; MS; m/z (relative intensity): 407 [(M+1) $^+$, 100].

Compound 3i. 66% yield; mp $178\text{--}180^\circ\text{C}$. [Found: C, 79.4; H, 8.3. $\text{C}_{34}\text{H}_{42}\text{O}_4$ requires C, 79.34; H, 8.22]; ν_{max} 1690, 1660, 1260, 700, 610 cm^{-1} ; δ_{H} 0.83 (s, 3H, steroidal- CH_3), 0.90 (s, 3H, steroidal- CH_3), 1.00–1.90 (m, 15H, steroidal- H), 2.39 (s, 3H, furanyl- CH_3), 2.55 (s, 3H, COCH_3), 2.57 (s, 2H, $=\text{C}-\text{CH}_2$), 4.95 (m, 1H, OCH), 5.89 (bs, 1H, $=\text{C}-\text{H}$), 6.30 (s, 1H, furanyl- H), 6.01–6.06 (m, 2H, Ar- H), 7.41–7.53 (m, 3H, Ar- H); δ_{C} 12.3, 14.4, 18.9, 21.1, 24.7, 27.5, 29.1, 29.8, 31.8, 34.0, 35.2, 35.6, 35.7, 36.7, 44.7, 45.3, 54.1, 54.4, 74.1, 105.7, 106.3, 122.8, 128.2, 129.4, 130.8, 132.6, 152.0, 155.9, 156.3, 166.0, 194.2; MS; m/z (relative intensity): 515 [(M+1) $^+$, 100].

Compound 3j. 55% yield; mp $59\text{--}60^\circ\text{C}$. [Found: C, 77.6; H, 6.2. $\text{C}_{19}\text{H}_{18}\text{O}_3$ requires C, 77.53; H, 6.16]; ν_{max} 1720, 1600, 680 cm^{-1} ; δ_{H} 1.27 (t, $J=7.1$ Hz, 3H, CH_2CH_3), 2.47 (s, 3H, furanyl- CH_3), 4.07 (s, 2H, Ar- CH_2), 4.23 (q, $J=7.1$ Hz, 2H, OCH_2), 6.27 (s, 1H, furanyl- H), 7.31–7.47 (m, 3H, Ar- H), 7.64 (s, 1H, Ar- H), 7.74–7.81 (m, 3H, Ar- H); δ_{C} 13.7, 14.3, 34.3, 59.9, 107.2, 114.0, 125.6, 126.0, 127.1, 127.5, 127.6, 128.2, 132.3, 133.5, 134.9, 152.3, 158.3, 164.2; MS; m/z

(relative intensity): 294 (M^+ , 100), 266 (48), 249 (11), 205 (25).

Compound 3k. 93% yield; mp 49–50°C. [Found: C, 70.3; H, 5.1. $C_{20}H_{17}ClO_3$ requires C, 70.49; H, 5.03]; ν_{max} 1710, 1265, 735, 640 cm^{-1} ; δ_H 1.32 (t, $J=7.1$ Hz, 3H, CH_2CH_3), 3.88 (s, 2H, Ar- CH_2), 4.26 (q, $J=7.1$ Hz, 2H, OCH_2), 6.43 (s, 1H, furanyl- H), 7.20–7.39 (m, 5H, Ar- H), 7.40–7.43 (m, 2H, Ar- H), 7.92–7.95 (m, 2H, Ar- H); δ_C 14.2, 33.6, 60.4, 109.6, 114.4, 128.0, 128.2, 128.7, 129.1, 130.1, 132.6, 135.6, 152.8, 156.6, 163.5; MS; m/z (relative intensity): 342 [$(M+2)^+$, 34] 340 (M^+ , 100), 311 (26), 295 (21), 105 (27), 77 (14).

Compound 3l. 31% yield; mp 60–61°C. [Found: C, 80.7; H 5.7. $C_{20}H_{24}O_3$ requires C, 80.88; H, 5.66]; ν_{max} 1710, 1280, 670 cm^{-1} ; δ_H 1.28 (t, $J=7.1$ Hz, 3H, CH_2CH_3), 4.16 (s, 2H, Ar- CH_2), 4.27 (q, $J=7.1$ Hz, 2H, OCH_2), 6.45 (s, 1H, furanyl- H), 7.35–7.48 (m, 6H, Ar- H), 7.71–7.79 (m, 4H, Ar- H), 7.83–7.98 (m, 2H, Ar- H); δ_C 14.2, 34.4, 60.4, 109.6, 114.4, 125.6, 126.1, 127.1, 127.2, 127.8, 128.0, 128.2, 128.3, 129.0, 129.5, 129.8, 132.3, 133.5, 153.4, 156.5, 163.6; MS; m/z (relative intensity): 356 (M^+ , 100), 327 (22), 311 (13), 105 (40), 77 (15).

Compound 3m. 35% yield; oil. [Found: C, 80.6; H 5.6. $C_{20}H_{24}O_3$ requires C, 80.88; H, 5.66]; ν_{max} (neat) 1705, 1250, 670 cm^{-1} ; δ_H 1.24 (t, $J=7.1$ Hz, 3H, CH_2CH_3), 4.20 (q, $J=7.1$ Hz, 2H, OCH_2), 4.43 (s, 2H, Ar- CH_2), 6.32 (s, 1H, furanyl- H), 7.35–7.52 (m, 8H, Ar- H), 7.77–8.06 (m, 4H, Ar- H); δ_C 14.1, 31.7, 60.3, 109.7, 114.5, 123.7, 125.5, 126.2, 127.1, 127.7, 127.9, 128.1, 128.7, 129.0, 129.3, 131.7, 133.8, 153.1, 156.2, 163.6; MS; m/z (relative intensity): 356 (M^+ , 100).

Compound 3n. 48% yield; mp 95–96°C. [Found: C, 77.5; H, 4.8; N, 3.76. $C_{24}H_{18}FNO_2$ requires C, 77.61; H, 4.88; N, 3.77]; ν_{max} 3300, 1710, 1600, 750, 680 cm^{-1} ; δ_H 3.90 (s, 2H, Ar- CH_2), 6.35 (s, 1H, furanyl- H), 7.06–7.74 (m, 14H, Ar- H); δ_C 30.8, 108.5, 115.4, 119.8, 127.1, 127.6, 128.3, 128.6, 128.9, 129.1, 129.5, 130.0, 130.3, 131.6, 154.0, 159.3, 164.1, 166.0; MS; m/z (relative intensity): 372 [$(M+1)^+$, 36], 280 (100).

Compound 3n'. 35% yield; mp 92–94°C. [Found: C, 77.8; H, 4.8; N, 3.79. $C_{24}H_{18}FNO_2$ requires C, 77.61; H, 4.88; N, 3.77]; ν_{max} 3350, 1685, 1600, 730, 680 cm^{-1} ; δ_H 3.89 (s, 2H, Ar- CH_2), 6.27 (s, 1H, furanyl- H), 7.04–7.77 (m, 14H, Ar- H), 10.68 (s, 1H, NH); δ_C 33.3, 99.8, 115.6, 118.5, 126.7, 127.9, 128.3, 129.4, 131.6, 132.8, 131.6, 144.7, 160.1, 164.2, 188.0; MS; m/z (relative intensity): 371 (M^+ , 100).

Compound 3o. 60% yield; mp 162–164°C. [Found: C, 82.8; H, 6.9. $C_{44}H_{44}O_4$ requires C, 82.99; H, 6.96]; ν_{max} 1730, 1670, 1620, 1280, 720 cm^{-1} ; δ_H 0.92 (s, 3H, steroidal- CH_3), 0.95 (s, 3H, steroidal- CH_3), 1.25–2.00 (m, 20H, steroidal- H), 2.38 (s, 2H, $=C-CH_2$), 4.75 (t, $J=7.6$ Hz, 1H, OCH), 5.40 (d, $J=3.4$ Hz, 1H, $=C-H$), 6.30 (s, 1H, furanyl- H), 8.09–7.25 (m, 15H, Ar- H); δ_C 11.9, 12.3, 13.4, 20.7, 22.6, 23.6, 27.7, 28.0, 28.8, 30.9, 31.4, 32.0, 34.7, 35.3, 38.3, 42.0, 45.0, 50.8, 53.5, 83.3, 109.7, 111.3, 124.4, 126.7, 127.2, 128.2, 128.5, 128.6, 128.8, 130.7, 132.7,

133.1, 138.1, 147.1, 147.3, 165.2, 166.5, 191.9; MS; m/z (relative intensity): 561 (5), 261 (100), 105 (100).

Compound 3p. 54% yield; mp 85–87°C. [Found: C, 84.5; H, 5.5. $C_{23}H_{18}O_2$ requires C, 84.64; H, 5.56]; ν_{max} 1650, 680, 660 cm^{-1} ; δ_H 2.46 (s, 3H, furanyl- CH_3), 4.07 (s, 2H, Ar- CH_2), 6.24 (s, 1H, furanyl- H), 7.37–7.89 (m, 12H, Ar- H); δ_C 13.6, 34.3, 108.3, 127.0, 127.6, 127.8, 128.0, 128.2, 128.8, 130.6, 131.4, 132.3, 135.5, 134.8, 139.2, 152.2, 158.7, 191.3; MS; m/z (relative intensity): 326 (M^+ , 100).

Compound 3p'. 24% yield; mp 80–82°C. [Found: C, 84.4; H, 5.4. $C_{23}H_{18}O_2$ requires C, 84.64; H, 5.56]; ν_{max} 1680, 680 cm^{-1} ; δ_H 2.31 (s, 3H, $COCH_3$), 4.14 (s, 2H, Ar- CH_2), 6.35 (s, 1H, furanyl- H), 7.37–7.88 (m, 12H, Ar- H); δ_C 29.7, 34.4, 109.0, 127.5, 127.8, 127.9, 128.1, 128.4, 128.8, 129.1, 129.4, 130.0, 132.3, 133.3, 133.5, 134.4, 138.2, 153.8, 155.7, 194.1; MS; m/z (relative intensity): 326 (M^+ , 100), 311 (35).

Compound 3q. 60% yield; mp 69–72°C. [Found: C, 81.9; H, 8.0. $C_{30}H_{40}O_3$ requires C, 82.22; H, 8.12]; ν_{max} 1710, 1670, 700 cm^{-1} ; δ_H 0.58 (s, 3H, steroidal- CH_3), 0.85 (s, 3H, steroidal- CH_3), 0.97–2.01 (m, 19H, steroidal- H), 2.06 (s, 3H, furanyl- CH_3), 2.39 (s, 3H, $COCH_3$), 2.41 (s, 2H, $=C-CH_2$), 5.32 (bs, 1H, $=C-H$), 5.73 (s, 1H, $=C-H$), 6.15 (s, 1H, furanyl- H), 7.32–7.47 (m, 3H, Ar- H), 7.69–7.66 (m, 2H, Ar- H); δ_C 12.3, 13.2, 17.8, 20.0, 21.7, 23.3, 24.8, 28.6, 30.5, 30.6, 34.7, 37.8, 43.0, 47.1, 56.0, 62.6, 108.4, 121.5, 125.2, 127.2, 127.9, 128.3, 130.9, 131.3, 138.2, 140.3, 150.5, 191.0, 208.5; MS; m/z (relative intensity): 497 [$(M+1)^+$, 100].

Compound 3q'. 19% yield; mp 135–140°C. [Found: C, 82.4; H, 8.2. $C_{30}H_{40}O_3$ requires C, 82.22; H, 8.12]; ν_{max} 1720, 1690, 690 cm^{-1} ; δ_H 0.72 (s, 3H, steroidal- CH_3), 0.94 (s, 3H, steroidal- CH_3), 1.13–1.72 (m, 19H, steroidal- H), 2.13 (s, 3H, $COCH_3$), 2.38 (s, 3H, $COCH_3$), 3.39 (s, 2H, $=C-CH_2$), 5.42 (bs, 1H, $=C-H$), 5.84 (s, 1H, $=C-H$), 6.43 (s, 1H, furanyl- H), 7.39–7.43 (m, 3H, Ar- H), 7.83–7.88 (m, 2H, Ar- H); δ_C 12.3, 17.9, 20.8, 21.7, 23.3, 25.0, 28.6, 28.7, 30.5, 30.6, 30.7, 33.0, 34.8, 37.8, 43.1, 47.1, 56.0, 62.6, 107.6, 124.4, 121.7, 125.5, 127.3, 127.9, 128.3, 130.9, 140.3, 152.4, 193.2, 208.6; MS; m/z (relative intensity): 497 [$(M+1)^+$, 100].

Compound 3r. 66% yield; mp 73–75°C. [Found: C, 79.5; H, 5.1; N, 4.64. $C_{20}H_{15}NO_2$ requires C, 79.72; H, 5.02; N, 4.65]; ν_{max} 2200, 1680, 670, 650 cm^{-1} ; δ_H 2.60 (s, 3H, $COCH_3$), 4.06 (s, 2H, Ar- CH_2), 6.30 (s, 1H, furanyl- H), 7.34–8.14 (m, 9H, Ar- H); δ_C 28.6, 34.1, 109.9, 125.1, 128.6, 128.9, 129.0, 129.3, 132.5, 136.0, 141.7, 153.7, 159.2, 171.7, 197.7; MS; m/z (relative intensity): 301 (M^+ , 21), 300 (100).

Compound 4a. 74% yield; mp 103–105°C. [Found: C, 68.2; H, 4.8; N, 4.1. $C_{20}H_{17}NO_5$ requires C, 68.37; H, 4.88; N, 3.99]; ν_{max} 1720, 1600, 1590, 1520, 750, 680 cm^{-1} ; δ_H 1.25 (t, $J=8.0$ Hz, 3H, CH_2CH_3), 2.10 (s, 2H, $=CCH_2$), 4.22 (q, $J=8.0$ Hz, 2H, OCH_2), 5.01 (s, 1H, $=CH$), 7.38–7.42 (m, 3H, Ar- H), 7.78 (d, $J=8.1$ Hz, 2H, Ar- H), 7.81–7.85 (m, 2H, Ar- H), 8.06 (d, $J=8.1$ Hz, 2H, Ar- H); δ_C 14.1, 30.9, 49.2, 60.8, 110.8, 111.4, 124.0, 128.1, 128.4, 128.9, 129.5,

145.6, 146.3, 150.8, 151.6, 157.2, 163.0; MS; m/z (relative intensity): 351 (M^+ , 21), 350 (100), 322 (15), 105 (30), 77 (20).

3.1.2. Synthesis of 2-arylalkynyl-1,3-dicarbonyls 5a–b. A typical procedure is as follows: to a solution of **1a** (0.176 g, 1.27 mmol) in DMF (5 mL), methyl 4-iodobenzoate **2b** (0.278 g, 1.06 mmol), Et_3N (0.536 g, 5.30 mmol), CuI (0.004 g, 0.02 mmol), dppf (0.023 g, 0.042 mmol) and PdCl_2 (0.005 g, 0.042 mmol) were added. The reaction mixture was gently purged with nitrogen and stirred at 30°C under a nitrogen atmosphere. After 24 h, ethyl acetate and 0.1N HCl were added; the organic layer was separated, washed with water, dried (Na_2SO_4) and the solvent evaporated in vacuo. The residue was purified by flash chromatography (90/10 *n*-hexane/EtOAc) to give **5a**.

Compound 5a. 0.24 g, 85% yield; mp $78\text{--}80^\circ\text{C}$. [Found: C, 70.4; H, 6.0. $\text{C}_{16}\text{H}_{16}\text{O}_4$ requires C, 70.57; H, 5.92]; ν_{max} 2200, 1710, 1600, 1260, 750, 680 cm^{-1} ; δ_{H} 2.29 (s, 6H, COCH_3), 2.95 (d, $J=7.5$ Hz, 2H, CHCH_2), 3.91 (s, 3H, OCH_3), 3.96 (t, $J=7.5$ Hz, 1H, CH_2CH), 7.40 (d, $J=6.6$ Hz, 2H, Ar-*H*), 7.96 (d, $J=6.6$ Hz, 2H, Ar-*H*); δ_{C} 14.1, 29.3, 52.0, 66.3, 82.0, 88.2, 127.5, 129.1, 129.7, 131.3, 166.2, 202.1; MS; m/z (relative intensity): 272 (M^+ , 8), 230 (100).

Compound 5b. 94% yield; oil. [Found: C, 75.6; H, 5.7. $\text{C}_{22}\text{H}_{20}\text{O}_4$ requires C, 75.84; H, 5.79]; ν_{max} (neat) 2200, 1730, 1680, 1260, 720, 660 cm^{-1} ; δ_{H} 1.66 (t, $J=7.1$ Hz, 3H, CH_2CH_3), 2.56 (s, 3H, COCH_3), 3.15 (dd, $J=6.1, 1.3$ Hz, 2H, CHCH_2), 4.19 (q, $J=7.1$ Hz, 2H, OCH_2), 4.68 (t, $J=6.1$ Hz, 1H, CH_2CH), 7.34 (d, $J=6.6$ Hz, 2H, Ar-*H*), 7.50–7.62 (m, 3H, Ar-*H*), 7.83 (d, $J=8.6$ Hz, 2H, Ar-*H*), 8.04–8.09 (m, 2H, Ar-*H*); δ_{C} 14.0, 19.5, 26.5, 53.0, 61.6, 81.9, 89.8, 126.1, 126.7, 128.8, 131.9, 133.8, 135.9, 168.3, 193.5, 197.3; MS; m/z (relative intensity): 249 [$(M+1)^+$].

Compound 6a. 63% yield; mp $103\text{--}105^\circ\text{C}$. [Found: C, 75.6; H, 5.7. $\text{C}_{22}\text{H}_{20}\text{O}_4$ requires C, 75.84; H, 5.79]; ν_{max} 1725, 1680 cm^{-1} ; δ_{H} 2.33 (s, 3H, furanyl- CH_3), 2.51 (s, 3H, COCH_3), 3.87 (s, 3H, OCH_3), 5.43 (s, 1H, Ar_3CH), 6.13 (s, 1H, furanyl-*H*), 7.14–7.31 (m, 7H, Ar-*H*), 7.98–8.02 (m, 2H, Ar-*H*); δ_{C} 14.3, 29.0, 50.5, 52.0, 109.2, 122.0, 127.4, 128.7, 128.9, 129.8, 129.9, 140.3, 142.6, 146.2, 151.4, 158.8, 166.7, 193.9; MS; m/z (relative intensity): 348 (M^+ , 100), 333 (24), 317 (15), 305 (17).

Compound 6b. 70% yield; mp $106\text{--}110^\circ\text{C}$. [Found: C, 79.6; H, 7.0. $\text{C}_{41}\text{H}_{44}\text{O}_5$ requires C, 79.84; H, 7.19]; ν_{max} 1740, 1720, 1690, 1610, 710, 690 cm^{-1} ; δ_{H} 0.90 (s, 3H, steroidal- CH_3), 0.93 (t, $J=7.1$ Hz, 3H, CH_2CH_3), 1.21–2.00 (m, 17H, steroidal-*H*), 2.59 (s, 3H, COCH_3), 4.27 (q, $J=7.1$ Hz, 2H, OCH_2), 4.80 (s, 1H, $=\text{C}(\text{Ar}_2)\text{CH}$), 5.38 (bs, 1H, $=\text{CH}$), 5.71 (s, 1H, $=\text{CH}$), 6.42 (s, 1H, furanyl-*H*), 7.34–7.40 (m, 5H, Ar-*H*), 7.89–8.01 (m, 4H, Ar-*H*); δ_{C} 13.6, 14.2, 19.0, 20.3, 21.7, 25.7, 26.6, 30.7, 31.4, 34.0, 34.9, 35.8, 47.6, 48.3, 51.7, 51.9, 60.5, 111.0, 114.4, 123.5, 127.7, 128.0, 129.2, 134.9, 136.0, 141.2, 145.3, 153.8, 163.5, 197.7, 220.9; MS; m/z (relative intensity): 616 (M^+ , 100), 587 (40).

3.1.3. 3-Acetyl-7-deuterio-hex-5-yn-2-one 7. To a stirred mixture of NaH (0.24 g, 6.07 mmol) and 3-acetyl-hex-5-yn-2-one **1a** (0.70 g, 5.06 mmol) in anhydrous THF (5 mL) was

added dropwise, under nitrogen atmosphere, a solution of *n*-BuLi (1.6 M) in hexanes (6.25 mL). The reaction mixture was stirred under a nitrogen atmosphere at rt. After 0.5 h, trifluoroacetic acid-*d* (1 mL) was added. Then, ethyl acetate and HCl 0.1 M were added, the organic layer was washed with water, dried (Na_2SO_4) and the solvent evaporated in vacuo. The residue was purified by chromatography (85/15 *n*-hexane/EtOAc) to afford the deuterated and the undeuterated product in 40% yield (0.28 g). 3-Acetyl-7-deuterio-hex-5-yn-2-one was determined by ^1H NMR and MS. From these analyses an abundance of D of approximately 70% was calculated.

Compound 8. 47% yield; δ_{H} 2.31 (s, 3H, furanyl- CH_3), 2.34 (s, 3H, COCH_3), 3.90 (s, 1.3H, CDH), 3.94 (s, 3H, OCH_3), 6.23 (s, 1H, furanyl-*H*), 7.27–7.31 (m, 2H, Ar-*H*), 7.96–8.00 (m, 2H, Ar-*H*); δ_{C} 14.1, 29.2, 33.8 (t, $^1J_{\text{C,D}}$ 21.1 Hz), 107.3, 128.8, 128.9, 142.7, 151.4, 157.7, 166.9, 194.1; MS; m/z (relative intensity): 274 [$(M+1)^+$, 100], 273 (M^+ , 70), 258 (95).

3.1.4. Synthesis of furans 9a–e (procedure C). A typical procedure is as follows: to a solution of **1a** (0.2 g, 1.45 mmol) in anhydrous acetonitrile were added 4-chlorophenyl iodide **2a** (0.23 g, 0.96 mmol), K_2CO_3 (0.67 g, 4.82 mmol), $\text{P}(o\text{-tol})_3$ (0.059 g, 0.19 mmol) and $\text{Pd}(\text{OAc})_2$ (0.011 g, 0.05 mmol). The flask was purged with carbon monoxide for a few seconds and connected to a balloon of carbon monoxide. The reaction mixture was stirred at 60°C overnight and poured in a separatory funnel containing 0.1N HCl and ethyl acetate. The organic layer was separated and the aqueous layer was extracted twice with ethyl acetate. The combined organic layers were dried (Na_2SO_4) and the solvent was evaporated in vacuo. The residue was purified by flash chromatography (85/15 *n*-hexane/EtOAc) to give 0.169 g (64% yield) of **9a**.

Compound 9a. Mp $108\text{--}109^\circ\text{C}$; lit. mp $109\text{--}110^\circ\text{C}$ and data consistent with that reported in the literature.¹³

Compound 9b. 55% yield; mp $83\text{--}85^\circ\text{C}$. [Found: C, 69.1; H, 5.1. $\text{C}_{15}\text{H}_{13}\text{FO}_3$ requires C, 69.22; H, 5.03]; ν_{max} 1720, 1690, 650, 620 cm^{-1} ; δ_{H} 2.37 (s, 3H, furanyl- CH_3), 2.55 (s, 3H, COCH_3), 4.27 (s, 2H, COCH_2), 6.51 (s, 1H, furanyl-*H*), 7.30–7.61 (m, 4H, Ar-*H*); δ_{C} 14.2, 28.8, 37.8, 109.1, 115.0 (d, $J=22.4$ Hz), 120.5 (d, $J=22.4$ Hz), 124.1, 130.3, 137.9, 145.6, 157.9, 162.6 (d, $J=250.4$ Hz), 193.3, 193.8; MS; m/z (relative intensity): 260 (M^+ , 81), 137 (65), 123 (100), 95 (39).

Compound 9c. 53% yield; mp $87\text{--}89^\circ\text{C}$. [Found: C, 68.1; H, 5.3. $\text{C}_{17}\text{H}_{16}\text{O}_5$ requires C, 67.99; H, 5.37]; ν_{max} 1720, 1690, 1260, 740, 670 cm^{-1} ; δ_{H} 2.37 (s, 3H, furanyl- CH_3), 2.55 (s, 3H, COCH_3), 3.95 (s, 3H, OCH_3), 4.32 (s, 2H, COCH_2), 6.52 (s, 1H, furanyl-*H*), 8.03–8.16 (m, 4H, Ar-*H*); δ_{C} 14.3, 29.1, 38.1, 109.3, 122.3, 128.3, 129.9, 134.2, 139.1, 145.7, 155.0, 165.8, 193.9, 194.8; MS; m/z (relative intensity): 300 (M^+ , 7), 163 (100), 137 (21).

Compound 9d. 60% yield; mp $83\text{--}85^\circ\text{C}$. [Found: C, 74.2; H, 5.9. $\text{C}_{15}\text{H}_{14}\text{O}_3$ requires C, 74.36; H, 5.82]; ν_{max} 1700, 1680, 750 cm^{-1} ; δ_{H} 2.37 (s, 3H, furanyl- CH_3), 2.55 (s, 3H, COCH_3), 4.28 (s, 2H, COCH_2), 6.50 (s, 1H, furanyl-*H*),

7.49–7.60 (m, 3H, Ar-*H*), 7.98–8.03 (m, 2H, Ar-*H*); δ_{C} 14.3, 29.1, 37.8, 109.1, 122.3, 128.4, 128.7, 133.6, 135.9, 146.2, 158.0, 194.1, 194.5; MS; m/z (relative intensity): 243[(M+1)⁺, 30], 105 (100).

Compound 9e. 60% yield; mp 65–67°C. [Found: C, 74.8; H, 6.2. C₁₆H₁₆O₃ requires C, 74.98; H, 6.29]; ν_{max} 1680, 1660, 720, 670 cm⁻¹; δ_{H} 2.35 (s, 3H, Ar-CH₃), 2.42 (s, 3H, furanyl-CH₃), 2.55 (s, 3H, COCH₃), 4.26 (s, 2H, COCH₂), 6.49 (s, 1H, furanyl-*H*), 7.20–7.40 (m, 2H, Ar-*H*), 7.78–7.82 (m, 2H, Ar-*H*); δ_{C} 14.3, 21.3, 29.1, 37.8, 109.0, 122.3, 125.7, 128.6, 128.9, 134.4, 136.0, 138.6, 146.3, 157.9, 194.1, 194.7; MS; m/z (relative intensity): 257 [(M+1)⁺, 8], 119 (100).

3.1.5. Synthesis of furans 9f–1 (procedure D). A typical procedure is as follows: to a 50 mL stainless steel autoclave charged with a solution of **1b** (0.186 g, 1.10 mmol) in anhydrous acetonitrile were added β -naphthyl triflate **2g** (0.203 g, 0.70 mmol), K₂CO₃ (0.51 g, 3.70 mmol) and Pd(PPh₃)₄ (0.040 g, 0.035 mmol). The autoclave was charged with carbon monoxide (2 atm) and the reaction mixture was stirred at 60°C overnight. Then, the mixture was poured in a separatory funnel containing 0.1N HCl and ethyl acetate. The organic layer was separated and the aqueous layer was extracted twice with ethyl acetate. The combined organic layers were dried (Na₂SO₄) and the solvent was evaporated in vacuo. The residue was purified by flash chromatography (80/20 *n*-hexane/EtOAc) to give 0.140 g (62% yield) of **9f**.

Compound 9f. Mp 155–157°C. [Found: C, 74.4; H, 5.6. C₂₀H₁₈O₄ requires C, 74.52; H, 5.63]; ν_{max} 1710, 1680, 1265, 660, 620 cm⁻¹; δ_{H} 1.18 (t, *J*=6.7 Hz, 3H, CH₂CH₃), 2.40 (s, 3H, furanyl-CH₃), 4.12 (q, *J*=6.7 Hz, 2H, OCH₂CH₃), 4.22 (s, 2H, COCH₂), 6.42 (s, 1H, furanyl-*H*), 7.42–7.87 (m, 6H, Ar-*H*), 8.51 (s, 1H, Ar-*H*); δ_{C} 13.7, 14.3, 38.0, 60.0, 109.3, 114.5, 127.8, 129.1, 130.0, 135.7, 146.2, 158.8, 164.0, 168.3, 194.5; MS; m/z (relative intensity): 322 (M⁺, 10), 155 (100), 127 (34).

Compound 9g. 62% yield; mp 60–62°C. [Found: C, 75.4; H, 7.8. C₃₆H₄₄O₆ requires C, 75.50; H, 7.74]; ν_{max} 1710, 1660, 1270, 750, 690 cm⁻¹; δ_{H} 0.73 (s, 3H, steroidal-CH₃), 0.94 (s, 3H, steroidal-CH₃), 1.32 (t, *J*=7.1 Hz, 3H, CH₂CH₃), 1.36–2.40 (m, 20H, steroidal-*H*), 2.53 (s, 3H, furanyl-CH₃), 3.93 (s, 2H, COCH₂), 4.25 (q, *J*=7.1 Hz, 2H, OCH₂CH₃), 4.95 (t, *J*=7.8 Hz, 1H, OCH₂CH₃), 6.41 (s, 1H, furanyl-*H*), 6.94 (bs, 1H, =CH), 7.43–7.55 (m, 3H, Ar-*H*), 8.02–8.06 (m, 2H, Ar-*H*); δ_{C} 12.0, 12.3, 12.4, 13.7, 14.3, 20.6, 23.6, 27.6, 28.2, 31.4, 34.4, 34.9, 35.2, 36.5, 36.9, 40.8, 42.9, 43.1, 46.9, 50.6, 53.5, 59.9, 108.7, 114.3, 128.3, 129.4, 130.6, 132.7, 137.5, 140.5, 147.0, 158.4, 164.0, 166.4, 195.2; MS; m/z (relative intensity): 573 [(M+1)⁺, 20], 527 (9), 451 (50), 405 (60), 105 (100).

Compound 9h. 50% yield; mp 108–111°C. [Found: C, 81.3; H, 9.8. C₃₆H₅₂O₃ requires C, 81.15; H, 9.84]; ν_{max} 1680, 1670 cm⁻¹; δ_{H} 0.71–2.16 (m, 41H, steroidal-*H*), 2.26 (s, 3H, furanyl-CH₃), 2.54 (s, 3H, COCH₃), 3.99 (s, 20H, COCH₂), 5.93 (bs, 1H, =CH), 6.41 (s, 1H, =CH), 7.01 (s, 1H, furanyl-*H*); δ_{C} 11.9, 14.3, 17.3, 18.7, 19.1, 20.7, 22.65, 23.8, 24.1, 28.0, 28.2, 29.1, 29.3, 31.7, 32.6, 33.1, 34.9,

35.7, 36.4, 39.5, 42.5, 48.1, 56.1, 56.7, 108.5, 122.3, 133.8, 134.3, 140.3, 141.8, 194.2, 195.3; MS; m/z (relative intensity): 533 [(M+1)⁺, 34], 395 (100), 137 (28).

Compound 9i. 57% yield; mp 144–146°C. [Found: C, 77.2; H, 7.8. C₂₈H₃₄O₄ requires C, 77.39; H, 7.89]; ν_{max} 1740, 1710, 1680 cm⁻¹; δ_{H} 0.93–2.19 (m, 23H, steroidal-*H*), 2.37 (s, 3H, furanyl-CH₃), 2.55 (s, 3H, COCH₃), 4.00 (s, 2H, COCH₂), 5.95 (bs, 1H, =CH), 6.42 (s, 1H, =CH), 7.04 (s, 1H, furanyl-*H*); δ_{C} 13.4, 14.1, 18.9, 20.1, 21.5, 28.9, 29.6, 30.1, 31.0, 31.1, 31.2, 34.8, 41.5, 51.5, 62.0, 108.4, 122.30, 132.8, 133.7, 139.8, 141.5, 148.9, 157.5, 193.0, 195.1, 220.4; MS; m/z (relative intensity): 435 [(M+1)⁺, 5], 297 (100).

3.1.6. Synthesis of vinyl esters 10a–e (procedure E). A typical procedure is as follows: to a solution of **1a** (0.21 g, 1.52 mmol) in anhydrous acetonitrile were added 4-chlorophenyl iodide **2a** (0.724 g, 3.04 mmol), K₂CO₃ (1.05 g, 7.60 mmol), P(*o*-tol)₃ (0.092 g, 0.30 mmol) and Pd(OAc)₂ (0.017 g, 0.08 mmol). The flask was purged with carbon monoxide for a few seconds and connected to a balloon of carbon monoxide. The reaction mixture was stirred at 60°C overnight and poured in a separatory funnel containing 0.1N HCl and ethyl acetate. The organic layer was separated and the aqueous layer was extracted twice with ethyl acetate. The combined organic layers were dried (Na₂SO₄) and the solvent was evaporated in vacuo. The residue was purified by flash chromatography (85/15 *n*-hexane/EtOAc) to give 0.320 g (51% yield) of **10a**.

Compound 10a. *E* isomer: mp 134–135°C; lit. mp 133–135°C and data consistent with that reported in the literature.¹³

Compound 10b. *E* isomer: (45% yield); mp 89–91°C. [Found: C, 69.3; H, 4.1. C₂₂H₁₆F₂O₄ requires C, 69.11; H, 4.22]; ν_{max} 1735, 1665, 760, 720 cm⁻¹; δ_{H} 2.27 (s, 3H, furanyl-CH₃), 2.30 (s, 3H, COCH₃), 6.64 (s, 1H, furanyl-*H*), 6.71 (s, 1H, =CH), 7.28–8.10 (m, 8H, Ar-*H*); δ_{C} 14.1, 28.8, 105.8, 111.3 (d, *J*=23.5 Hz), 111.8, 115.5, 115.7 (d, *J*=27.2 Hz), 117.1 (d, *J*=23.2 Hz), 120.1, 120.5 (d, *J*=36.8 Hz), 121.3, 122.9, 130.3, 130.5, 131.3, 136.6, 143.8, 147.1, 158.6, 162.7 (d, *J*=248.0 Hz), 163.1 (d, *J*=235.9 Hz), 193.5; MS; m/z (relative intensity): 382 (M⁺, 29), 123 (100).

Compound 10c. *E* isomer: (54% yield); mp 147–150°C. [Found: C, 67.3; H, 4.9. C₂₆H₂₂O₈ requires C, 67.53; H, 4.80]; ν_{max} 1720, 1675, 750, 700 cm⁻¹; δ_{H} 2.41 (s, 6H, furanyl-CH₃ and COCH₃), 3.91 (s, 3H, OCH₃), 3.99 (s, 3H, OCH₃), 6.68 (s, 1H, furanyl-*H*), 6.83 (s, 1H, =CH), 7.60 (BB' part of an AA'BB' system, *J*=8.5 Hz, 2H, Ar-*H*), 8.02 (AA' part of an AA'BB' system, *J*=8.5 Hz, 2H, Ar-*H*), 8.24 (BB' part of an AA'BB' system, *J*=8.7 Hz, 2H, Ar-*H*), 8.36 (AA' part of an AA'BB' system, *J*=8.7 Hz, 2H, Ar-*H*); δ_{C} 14.1, 28.8, 52.1, 52.5, 108.5, 112.2, 122.9, 129.9, 128.8, 128.9, 130.1, 132.7, 134.7, 138.1, 143.8, 147.0, 158.8, 163.8, 165.9, 168.2, 193.3; MS; m/z (relative intensity): 462 (M⁺, 4), 163 (100).

Compound 10d. *E* isomer: (40% yield); mp 85–86°C. [Found: C, 76.1; H, 5.2. C₂₂H₁₈O₄ requires C, 76.29; H,

5.24]; ν_{\max} 1710, 1670 cm^{-1} ; δ_{H} 2.24 (s, 3H, furanyl- CH_3), 2.33 (s, 3H, COCH_3), 6.64 (s, 1H, furanyl- H), 6.72 (s, 1H, $=\text{CH}$), 7.32–8.32 (m, 10H, Ar- H); δ_{C} 14.1, 28.8, 108.5, 110.7, 124.4, 127.1, 128.7, 128.9, 130.2, 133.8, 134.3, 145.4, 147.6, 158.2, 164.4, 193.7; MS; m/z (relative intensity): 346 (M^+ , 18), 105 (100).

Compound 10e. *E* isomer: (37% yield); mp 60–62°C. [Found: C, 76.8; H, 6.0. $\text{C}_{24}\text{H}_{22}\text{O}_4$ requires C, 76.99; H, 5.92]; ν_{\max} 1730, 1660, 760, 720 cm^{-1} ; δ_{H} 2.22 (s, 3H, furanyl- CH_3), 2.32 (s, 6H, ArCH_3), 2.44 (s, 3H, COCH_3), 6.62 (s, 1H, furanyl- H), 6.69 (s, 1H, $=\text{CH}$), 7.31–8.10 (m, 8H, Ar- H); δ_{C} 14.1, 21.2, 21.4, 28.7, 104.6, 110.6, 121.6, 122.8, 124.1, 125.0, 127.2, 127.3, 128.3, 128.6, 129.7, 130.6, 134.3, 134.6, 145.7, 158.1, 164.6, 193.4; MS; m/z (relative intensity): 374 (M^+ , 18), 119 (100).

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