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Cu-Catalyzed Reaction of 1,2-Dihalobenzenes with 1,3-Cyclohexanediones for the Synthesis of 3,4-Dihydrodibenzo[*b*,*d*]furan-1(2*H*)-ones

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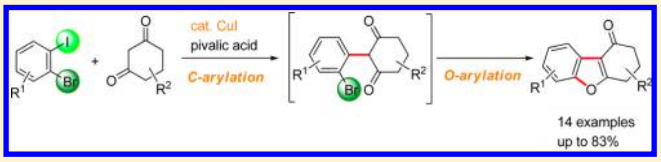
Supporting Information

ABSTRACT: The Cu(I)-catalyzed reaction of 1-bromo-2-iodobenzenes and other 1,2-dihalobenzenes with 1,3-cyclohexanediones in DMF at 130 °C using Cs_2CO_3 as a base and pivalic acid as an additive selectively delivers 3,4-dihydrodibenzo[*b*,*d*]furan-1(2*H*)-ones with yields ranging from 47 to 83%. The highly regioselective domino process is based on an intermolecular Ullmann-type *C*-arylation followed by an intramolecular Ullmann-type *O*-arylation. Substituted products are accessible by employing substituted 1-bromo-2-iodobenzenes and substituted 1,3-cyclohexanediones as substrates. Reaction with an acyclic 1,3-diketone yields the corresponding benzo[*b*]furan.



INTRODUCTION

Numerous molecules with a benzo[*b*]furan or a dibenzo[*b*,*d*]-furan skeleton[1] have been isolated from natural sources. Typical examples include the karnatakafurans A and B from *Aspergillus karnatakaensis* Frisvad,[2a] achyrofuran from *Achyrocline satureioides*,[2b] the porric acids A–C from *Allium porrum* L,[2c] popolohuanone E from a Pohnpei sponge *Dysidea* sp.,[2d] eriobofuran from *Eriobotrya japonica* L,[2e] and the *α*-, *β*-, and *γ*-pyrufurans from *Pyrus communis* L[2f,g] (Figure 1). Compounds that contain a dibenzo[*b*,*d*]furan structure element exhibit a wide range of biological activities including antimalarial,[2a] antimicrobial,[2a] antifungal,[2c,e] cytotoxic,[2d] antitubercular,[3a,b] and antimycobacterial properties.[3c,d]

There has been continuing interest in the development of novel synthetic methods for the efficient preparation of dibenzo[*b*,*d*]furans. Over the years, various routes have been reported for the synthesis of this skeleton. They include the ring closure of 2-phenoxybenzene diazonium salts which was first reported by Graebe and Ullmann,[4] intermolecular Diels–Alder reactions between 2- or 3-nitrobenzofurans and electron-rich dienes,[5] the reaction of benzofuran-3-ones with 2*H*-pyran-2-ones,[6] and the reaction of *o*-silyl aryltriflates with iodonium ylides.[7] More recently, the focus was on the development of methods based on transition-metal-catalyzed transformations. Among them are the Pd-catalyzed cyclization of 1-halo-2-phenoxybenzenes,[8] the Pd-catalyzed oxidative cyclization of diphenyl ethers,[9] the Pd- or Cu-catalyzed intramolecular *O*-arylation of 2-halobiphenyl-2′-ols,[10] the Pd- or Cu-catalyzed oxidative cyclization of 2-arylphenols,[11] the Pd-catalyzed intramolecular cyclization of 1-carboxyl-2-phenoxybenzenes,[12] and the Au-catalyzed reaction between *O*-arylhydroxylamines and 1,3-dicarbonyls.[13] Despite these advances, there is still a need for new methods that avoid the use of complex substrates, expensive reagents, additives, and catalysts and allow for the straightforward synthesis of dibenzo[*b*,*d*]furans from readily available starting materials. Recently, we reported on Cu-catalyzed domino reactions for the synthesis of a number of carbocycles and heterocycles,[14] such as the reaction between 2-halobenzyl halides and amidines for the preparation of quinazolines[14a] and the reaction between 2-halobenzyl halides and *β*-ketoesters for the synthesis of naphthalenes and 4*H*-chromenes.[14c] It was assumed that the synthesis of dibenzo-[*b*,*d*]furans could be achieved by a domino intermolecular *C*-arylation/intramolecular *O*-arylation of a 1,2-dihalobenzene and a 1,3-cyclohexanedione (I + II → III → IV) (Scheme 1). Needless to say, if successful, this approach could be extended to the synthesis of numerous other *O*-heterocyclic systems. The Cu-catalyzed reaction between 1,2-dihalobenzenes and 1,3-diketones has not been reported so far. However, Ma et al. have achieved the Cu-catalyzed reaction between 1,2-dihalobenzenes and *β*-ketoesters for the preparation of benzo[*b*]furans.[15]

In recent years, there was great interest in the transition-metal-catalyzed arylation of 1,3-dicarbonyls with aryl halides.[16] The Pd-catalyzed *C*-arylation of 1,3-dicarbonyls dates back to the 1980s[17] and has been further developed over the years.[18] Meanwhile, it is considered as a highly useful synthetic method. The only disadvantage of the Pd-catalyzed transformation is the need for expensive Pd reagents and ligands. This is the reason why there is a strong interest in replacing the Pd reagents by much cheaper Cu reagents. Early examples for the Cu-catalyzed arylation of 1,3-dicarbonyls include the reaction of

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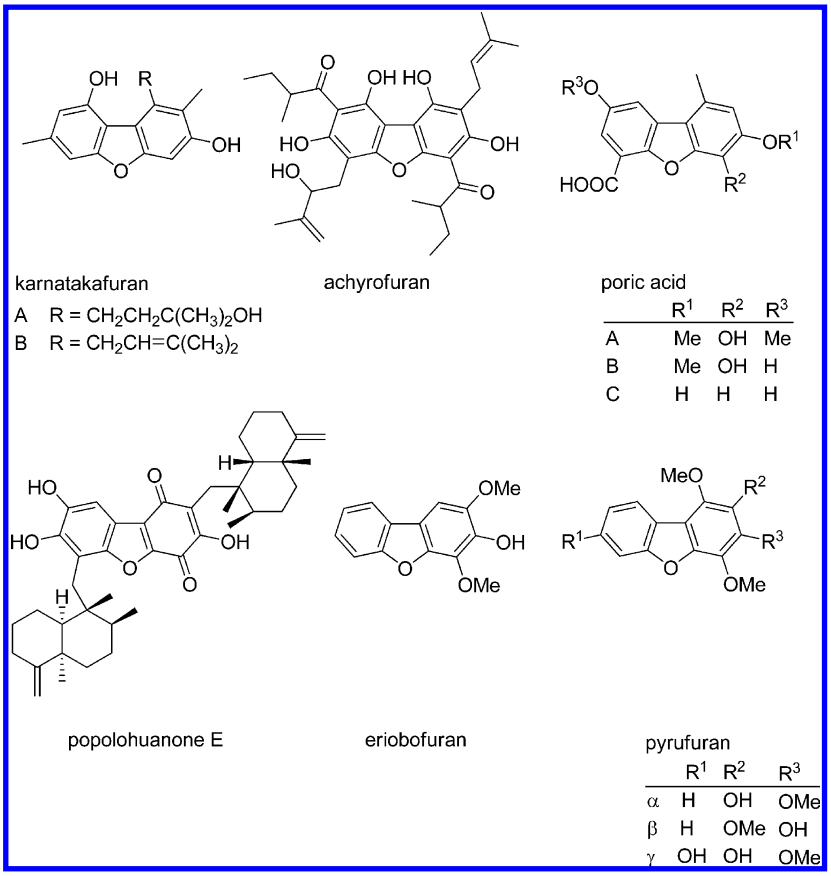
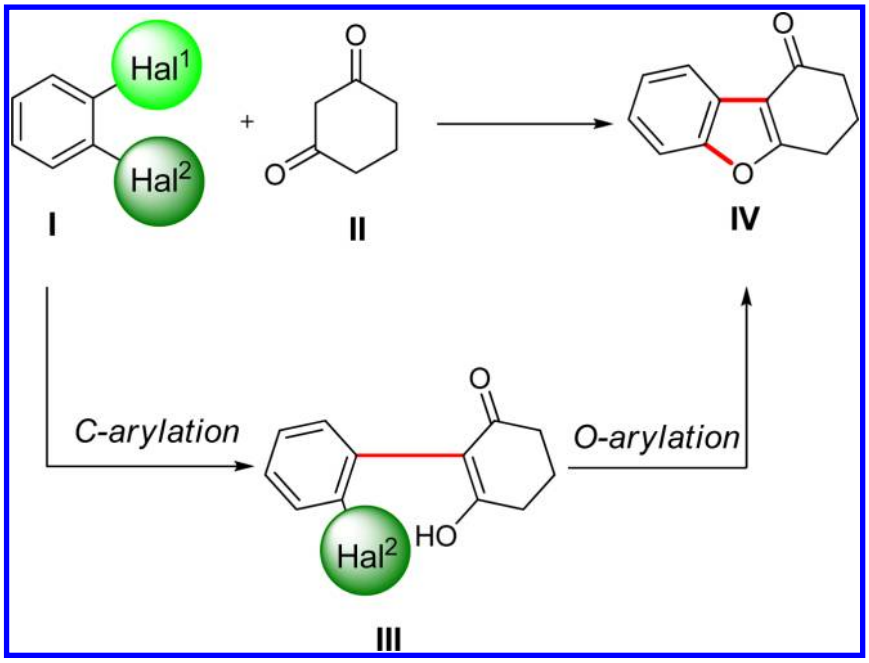


Figure 1. Selected natural products with a dibenzo[*b*,*d*]furan skeleton.

Scheme 1. Proposed Route for the Cu-Catalyzed Synthesis of 3,4-Dihydrodibenzo[*b*,*d*]furan-1(2*H*)-ones



o-bromobenzoic acid with several 1,3-dicarbonyls.[19] However, many of these transformations need comparably harsh reaction conditions, like high reaction temperatures and/or strong bases. Meanwhile, a number of protocols are known that allow for milder reaction conditions as well as better yields. Typical examples are the reactions of aryl iodides and aryl bromides with 1,3-dicarbonyls and related compounds, such as malonic esters, *β*-ketoesters, *β*-diketones, cyanoacetates, and malononitrile.[20] The scope of the Cu-catalyzed C-arylation of 1,3-dicarbonyls can be extended tremendously when they are combined with other transformations to new domino processes. Using this approach, a number of heterocycles can

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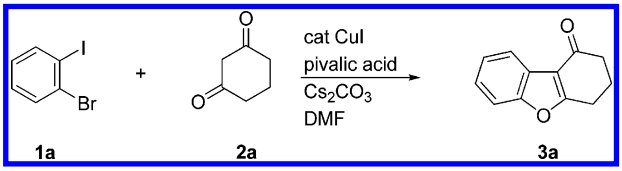
be synthesized efficiently. Typical examples are related to the preparation of *N*- and *O*-heterocycles such as indoles,[21] isoquinolines,[22] benzimidazoisoquinolines,[23] and 4*H*-chromenes.[14c]

Herein, we disclose a new and straightforward approach for the selective synthesis of dibenzo[*b*,*d*]furan derivatives that is based on the Cu-catalyzed domino reaction between 1,2-dihalobenzenes **1** and 1,3-cyclohexanediones **2**.

RESULTS AND DISCUSSION

The reaction between 1-bromo-2-iodobenzene (**1a**) and 1,3-cyclohexanedione (**2a**) was chosen as a model reaction. When 1 equiv of **1a** and 2 equiv of **2a** were reacted under the reaction conditions that have been developed by Ma et al. for the synthesis of substituted benzo[*b*]furans from 1-bromo-2-iodobenzenes **1** and acyclic *β*-ketoesters, i.e., 10 mol % of CuI, 3 equiv of K_2CO_3 in THF at 100 °C for 24 h, not even a trace of the desired dibenzo[*b*,*d*]furan was formed. Pivalic acid as an additive is known to improve the yield of several Pd-catalyzed inter- and intramolecular arylations that are based on the activation of C−H bonds.[24] Very recently, there was also a report on the Cu-catalyzed oxidative C(sp^2)−H cycloetherification of *o*-arylphenols using pivalic acid to facilitate the C−H bond activation.[11a] Although there was no hint for the use of pivalic acid as an additive in transition-metal-catalyzed reactions between aryl halides and 1,3-dicarbonyls, it seemed worthwhile to investigate the influence of pivalic acid on the Cu-catalyzed model reaction between **1a** and **2a**. When equimolar amounts of **1a** and **2a** were reacted in the presence of 10 mol % of CuI, 2 equiv of Cs_2CO_3, and 1.2 equiv of pivalic acid in DMF at 130 °C for 7 h, 3,4-dihydrodibenzo[*b*,*d*]-furan1(2-*H*)-one (**3a**) could be isolated in 16% yield (Table 1, entry 1). Encouraged by this result, further experiments were conducted. The yield of **3a** could easily be increased by extending the reaction time (Table 1, entries 2−5). When the experiment was run for 28 h, **3a** was isolated in 71% yield as the sole product (Table 1, entry 5).

Table 1. Optimization of the Reaction between 1-Bromo-2-iodobenzene (1a) and 1,3-Cyclohexanedione (2a) To Yield 3,4-Dihydrodibenzo[*b*,*d*]furan-1(2*H*)-one (3a)

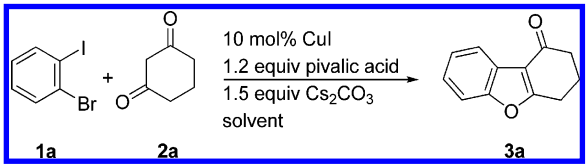


entry	molar ratio **1a**:**2a**	CuI (mol %)	pivalic acid (equiv)	Cs_2CO_3 (equiv)	*T* (°C)	time (h)	yield of **3a** (%)
1	1:1	10	1.2	2	130	7	16
2	1:1	10	1.2	2	130	16	51
3	1:1	10	1.2	2	130	20	61
4	1:1	10	1.2	2	130	24	64
5	1:1	10	1.2	2	130	28	71
6	1:1	5	1.2	2	130	28	59
7	1:1	15	1.2	2	130	28	71
8	1:1	20	1.2	2	130	28	68
9	1:1	10	0.6	2	130	28	47
10	1:1	10	1.8	2	130	28	70
11	1:1	10	1.2	1.5	130	28	72
12	1:1	10	1.2	3	130	28	52
13	1:1.5	10	1.2	1.5	130	28	75
14	1:2	10	1.2	1.5	130	28	69
15	1:1.5	10	1.2	1.5	100	36	69
16	1:1.5	10	1.2	1.5	150	28	55

Next, the influence of the amount of CuI on the outcome of the reaction was studied. The yield dropped from 71% to 59% when the reaction was run in the presence of 5 mol % of CuI (Table 1, entry 6). Remarkably enough, the yield could not be improved by increasing the amount of CuI to 15 mol % or even to 20 mol % (Table 1, entries 7 and 8). The effect of the amount of pivalic acid on the result of the reaction was also of interest. The use of 0.6 equiv of pivalic acid led to a significant 24% yield drop (Table 1, entry 9). Interestingly, an increase of the amount of pivalic acid to 1.8 equiv did not pay off as well (Table 1, entry 10). Furthermore, it was established that the amount of Cs_2CO_3 can be reduced to 1.5 equiv without affecting the yield (Table 1, entry 11). When the reaction was conducted with 3 equiv of Cs_2CO_3, the yield of **3a** decreased to 52% (Table 1, entry 12). The highest yield of **3a** (75%) was obtained when the amount of **2a** was increased from 1 to 1.5 equiv (Table 1, entry 13). A further increase of **2a** to 2 equiv did not pay off (Table 1, entry 14). Performing the reaction at 100 and 150 °C did not bring any improvement. Instead, the yield of **3a** dropped to 69% and 55%, respectively (Table 1, entries 15 and 16).

On the basis of the reaction conditions given in the Table 1, entry 13, the influence of different bases and solvents on the model reaction was investigated (Table 2). It was interesting to find that Cs_2CO_3 can be replaced with cheap bases like K_3PO_4 or K_2CO_3. Use of K_3PO_4 afforded **3a** with 70% yield (Table 2, entry 1), and with K_2CO_3 **3a** could be isolated with 62% yield (Table 2, entry 2). As expected, in the absence of any base no product was formed (Table 2, entry 3). The following experiments focused on the influence of the solvent. Therefore, the model reaction was run in a variety of different solvents (Table 2). It was observed that the transformation can be run not only in polar aprotic solvents like DMSO, DMA, CH_3CN, NMP, and 1-nitropropane but also in solvents like *i*-PrOH, THF, and $C_2H_4Cl_2$. The best yields were obtained with DMSO and DMA, but in no case the yield did exceed the yield obtained in DMF.

Table 2. Influence of Bases and Solvents on the Outcome of the Model Reaction 1a + 2a → 3a[a]



entry	base	solvent	*T* (°C)	time (h)	yield of **3a** (%)
1	K_3PO_4	DMF	130	28	70
2	K_2CO_3	DMF	130	28	62
3		DMF	130	24	
4	Cs_2CO_3	DMSO	130	24	74
5	Cs_2CO_3	DMA	130	28	71
6	Cs_2CO_3	CH_3CN	100	24	66
7	Cs_2CO_3	NMP	130	28	56
8	Cs_2CO_3	1-nitropropane	130	28	42
9	Cs_2CO_3	THF	100	24	52
10	Cs_2CO_3	*i*-PrOH	100	28	35
11	Cs_2CO_3	$C_2H_4Cl_2$	100	24	15

[a]In all cases, 1 equiv of **1a** was reacted with 1.5 equiv of **2a**.

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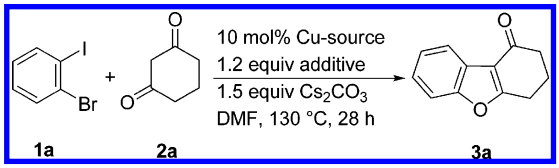
It was then studied whether other carboxylic acids than pivalic acid can be used as acidic additives (Table 3). The

Table 3. Influence of the Cu Source and Additives on the Outcome of the Model Reaction 1a + 2a → 3a



entry	additive	Cu source	yield of **3a** (%)
1	acetic acid	CuI	60
2	propionic acid	CuI	64
3	isovaleric acid	CuI	70
4	benzoic acid	CuI	46
5		CuI	
6	pivalic acid	CuCl	63
6	pivalic acid	CuBr	66
7	pivalic acid	CuCN	30
8	pivalic acid	Cu_2O	64
9	pivalic acid	Cu	32
10	pivalic acid		

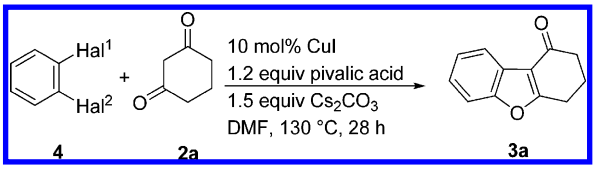
[a]In all cases, 1 equiv of **1a** was reacted with 1.5 equiv of **2a**.

model reaction could be performed with different carboxylic acids like acetic acid, propionic acid, isovaleric acid, and benzoic acid, but in all cases the yields were inferior compared to pivalic acid. A control experiment demonstrated that in the absence of an acidic additive not even a trace of **3a** was formed (Table 3, entry 5). Finally, we focused on the role of different Cu sources. For this purpose, the model reaction was run with several Cu(I) compounds as well as with elemental copper under the condition given in Table 1, entry 13. It was found that with CuBr, CuCl, and Cu_2O the yields of **3a** were higher than 60% and that **3a** was even formed with elemental copper as the Cu source. However, in no case did the yield exceed the yield obtained with CuI. A control experiment established that the domino reaction does not take place in the absence of a Cu source (Table 3, entry 10).

Control experiments clearly established that the reaction between **1a** and **2a** cannot be run successfully in the absence of a base (Table 2, entry 3), an acidic additive (Table 3, entry 5), and of course, a Cu source (Table 3, entry 10). In none of the three control experiments could the product **3a** be detected. After successful optimization of the reaction conditions, we began to study the scope of the domino process with respect to both the 1,2-dihalobenzene and the 1,3-dicarbonyl. First, we examined whether 1-bromo-2-iodobenzene (**1a**) can be replaced with other 1,2-dihalobenzenes (Table 4). The experiments revealed that **1a** can be replaced by 1,2-diiodobenzene (**4a**) and 1,2-dibromobenzene (**4b**) without any significant yield loss of **3a**. 1,2-Dichlorobenzene (**4c**) can also be used as a substrate for the Cu(I)-catalyzed dibenzofuran synthesis. However, the yield of **3a** was much lower (Table 4, entry 3). All further reactions were conducted with 1-bromo-2-iodobenzenes as the substrate. This was not only because of the excellent yields obtained with **1a** but also because only the use of a mixed 1,2-dihalobenzene opens the possibility for regioselective reactions with substituted dihalobenzenes.

To study the scope of the dibenzofuran synthesis, the reaction of 1-bromo-2-iodobenzene (**1a**) was carried out with a

Table 4. Reactions of Different 1,2-Dihalobenzenes 4 with 1,3-Cyclohexanedione (2a)[a]



entry	**4**	Hal^1	Hal^2	yield of **3a** (%)
1	**a**	I	I	72
2	**b**	Br	Br	70
3	**c**	Cl	Cl	40

[a]In all cases, 1 equiv of **4** was reacted with 1.5 equiv of **2a**.

number of mono- and disubstituted 1,3-cyclohexanediones **2b–h**. The results are summarized in Table 5. With most 1,3-cyclohexanediones (i.e., **2b–e,h,i**), the domino reaction delivered the corresponding dihydrodibenzo[*b,d*]furan-1(2*H*)-ones **3** exclusively. The yields were in the range between 62 and 80% (Table 5, entries 1–4 and 7). Surprisingly, with 5-(4-methoxyphenyl)-1,3-cyclohexanedione (**2f**) and with 5-(4-chlorophenyl)-1,3-cyclohexanedione (**2g**) as the substrates not a trace of the expected dihydrodibenzo[*b,d*]furan-1(2*H*)-ones was formed. Instead, the corresponding unsaturated dibenzo[*b,d*]furan-1-ols **3f** and **3g** were isolated in 64% and 61% yield, respectively. So far, the reasons for the occurrence of the oxidized products remain unclear. In addition to the 1,3-cyclohexanediones the reaction was also run with 2,4-pentanedione (**2i**) as the 1,3-dicarbonyl to yield 1-(2-methylbenzofuran-3-yl)ethanone (**3i**) with 83% yield. This experiment proved that the domino reaction is not restricted to cyclic 1,3-dicarbonyls.

As a control experiment, the reaction between **1a** and the acyclic *β*-diketone **2i** was conducted under the conditions developed for the reaction of **1a** with *β*-ketoesters in Ma's laboratory, i.e., 10 mol % of CuI, 3 equiv of K_2CO_3, THF, 100 °C, 24 h (Scheme 2). Under these conditions, not even a trace of the expected product **3i** was formed. This result emphasizes that the success of Cu(I)-catalyzed domino processes with different types of 1,3-dicarbonyls often depends on the careful choice of catalysts, additives, solvents, and reaction conditions. On the other hand, when **1a** was reacted with ethyl acetoacetate (**5**) under the conditions optimized for cyclic *β*-diketones **2** the corresponding ethyl 2-methylbenzofuran-3-carboxylate (**6**) was isolated in 63% yield (Scheme 2).

Then, the scope of the dibenzo[*b,d*]furan synthesis with respect to the 1-bromo-2-iodobenzenes was studied (Table 6). For this purpose, several 1-bromo-2-iodobenzenes with an additional substituent in the 4- or 5-position were reacted with 1,3-cyclohexanedione (**2a**). The corresponding dihydrodibenzo[*b,d*]furans **3j–n** were isolated with yields ranging from 47 to 77%. In all cases, the domino process proceeds highly regioselective, i.e., only a single regioisomer was formed. With *o*-bromoiodobenzenes **1c,d,f** carrying an additional substituent in the *para*-position to iodine, only the 7-substituted products **3k,l,n** were formed. The *meta*-substituted substrates **1b** and **1e** delivered exclusively the 8-substituted products **3j** and **3m**.

The high regioselectivity of the transformation requires that the first step of the domino process is either a C,C-bond formation between the C–I bond of **1b–f** and C-2 of the 1,3-diketone **2a** or a C,O-bond formation between the C–Br bond

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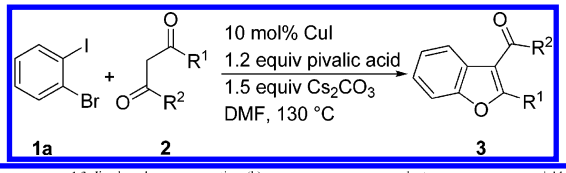
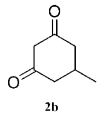
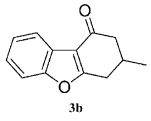
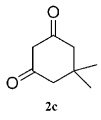
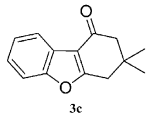
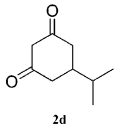
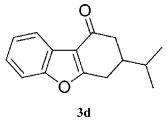
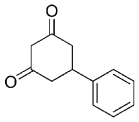
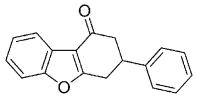
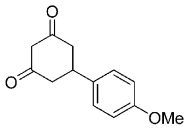
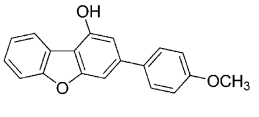
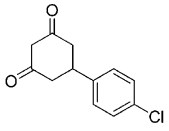
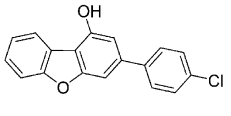
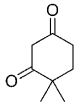
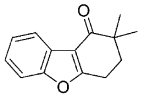
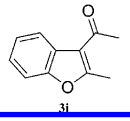
Table 5. Reaction of 1-Bromo-2-iodobenzene (1a) with Different 1,3-Dicarbonyls 2[a]



entry	1,3-dicarbonyl	time (h)	product	yield 3 (%)
1	 2b	20	 3b	78
2	 2c	24	 3c	80
3	 2d	22	 3d	80
4	 2e	24	 3e	62
5	 2f	26	 3f	64
6	 2g	22	 3g	61
7	 2h	24	 3h	78
8	 2i	22	 3i	83

[a]In all cases, 1 equiv of **1a** was reacted with 1.5 equiv **2**.

of **1b**–**f** and an oxygen atom of the 1,3-dicarbonyl **2a**. To explore the mechanistic alternatives, two control experiments were performed; i.e., the reactions between iodobenzene (**7a**) and bromobenzene (**7b**) with acetylacetone (**2i**) (Scheme 3). Both reactions were performed under our optimized reaction conditions for 3 and 4.5 h, respectively. In both experiments, only **8**, i.e., the *C*-arylation product, was formed. Not even a trace of the corresponding *O*-arylation product was isolated. This is a clear indicator that the C,C-bond formation between **1** and **2** takes place as the first step of the formation of **3**.

This result also supports the view that the new C,C bond originates from the reaction between the C–I bond of **1a** and C-2 of the 1,3-diketone **2a**. This assumption requires that the C–Br bond is less reactive than the C–I bond. Therefore, a competition experiment between **7a**/**7b** and **2i** was performed. For this purpose, a 1:1 mixture of **7a** (1 mmol) and **7b**

Scheme 2. Reaction of 1a with 2i and 5 under Different Reaction Conditions

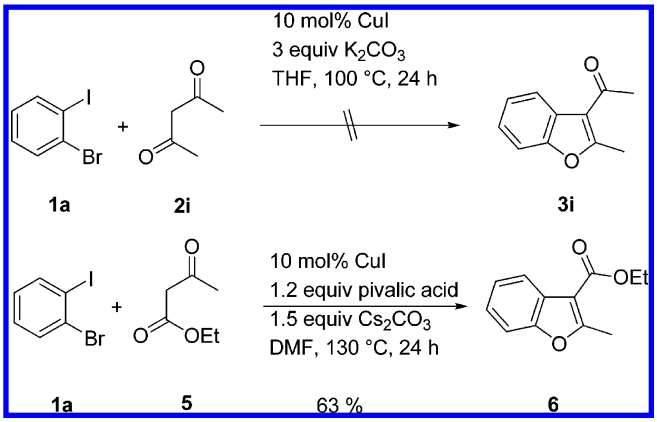
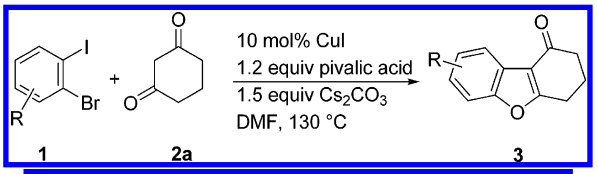
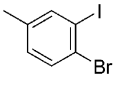
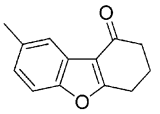
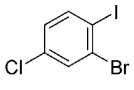
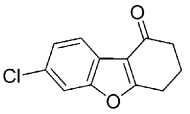
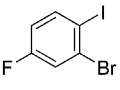
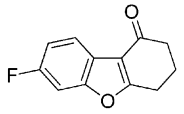
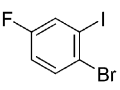
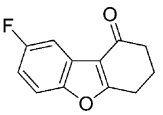
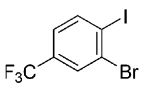
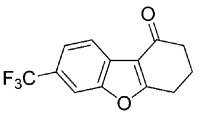


Table 6. Reaction of 1,3-Cycohexanedione (2a) with Different 1-Bromo-2-iodobenzenes 1[a]



entry	1	time (h)	product	yield 3 (%)
1	 1b	23	 3j	77
2	 1c	20	 3k	71
3	 1d	20	 3l	66
4	 1e	20	 3m	64
5	 1f	28	 3n	47

[a]In all cases, 1 equiv **1** was reacted with 1.5 equiv **2a**.

(1 mmol) was reacted with **2i** (1 mmol) under the conditions of our optimized protocol. After 5 h, 58% of **8** and 28% of a mixture of **7a** and **7b** in a 24:76 ratio were isolated. These results clearly indicate that the C–I bond of **7a** is much more reactive than the C–Br bond of **7b**. In summary, the results obtained strongly support the view that the first step of the domino process proceeds as an intermolecular C,C-bond formation between C-2 of the 1,3-diketone and the aromatic carbon atom carrying the iodo substituent. The second step is an intramolecular C,O-bond formation between an O-atom of

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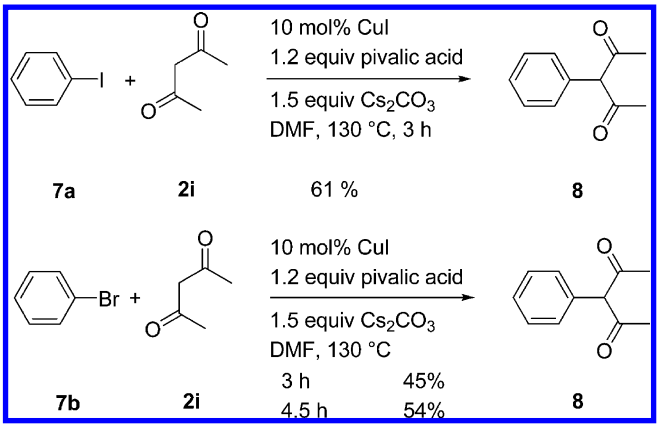
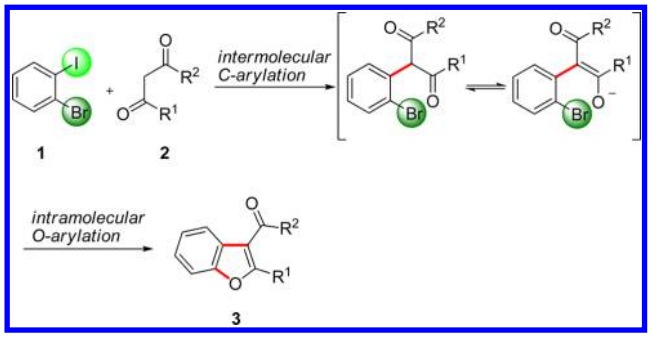
Scheme 3. Reactions between Iodobenzene (7a) and Bromobenzene (7b) with Acetylacetone (2i)



Scheme 4. Proposed Reaction Mechanism



the 1,3-dicarbonyl and the aromatic carbon carrying the bromo atom (Scheme 4).

The structures of all compounds were unambiguously elucidated by NMR spectroscopy and mass spectrometry. Structure elucidation of all compounds and full assignment of the ^{1}H and ^{13}C chemical shifts were achieved by evaluating their gCOSY, gHSQC, and gHMBC spectra. For example, compound **3j** contains two scalar coupled ^{1}H spin systems, one consisting of alicyclic protons at C-2,C-3 and C-4-H (ring A) and the other of aromatic protons 6-H, 7-H, 9-H (ring B). The sequence of the protons in both spin systems was determined by analysis of the gCOSY spectrum. To prove the proposed structure, we used gHMBC optimized for $^{3}J_{CH}$ = 8 Hz to fix the positions of the six quaternary carbons C-1, C-4a, C-5a, C-8, C-9a, and C-9b. Carbon C-9b showed strong ^{3}J-HMBC correlations to protons 2-H, 4-H, and 9-H, C-9a to proton 6-H, C-5a to protons 7-H and 9-H, C-1′ to protons 9-H and 7-H as well as C-4a to 3-H. These findings established that the two rings A and C are linked by the four carbons C-4a, C-9b, C-9a, and C-5a as shown in Figure 2.

Unequivocal evidence for the structure of the **3j** was produced by X-ray structure analysis. For this purpose, crystals of **3j** were studied by X-ray crystal structure analysis (see the Supporting Information).[25]

CONCLUSIONS

In summary, we have developed a simple and efficient method for the regioselective preparation of 3,4-dihydro[*b*,*d*]furan-1(2*H*)-ones by reaction between 1-bromo-2-iodobenzenes **1** and 1,3-cyclohexanediones **2**. The CuI-catalyzed reaction is regarded as a domino intermolecular Ullmann *C*-arylation/intramolecular Ullmann *O*-arylation that delivers the products with high selectivity and with yields ranging from 47 to 83%. The domino process can also be achieved with 1,2-diiodobenzene and 1,2-dibromobenzene as the aromatic substrate and with acetylacetone or ethyl acetoacetate as the 1,3-dicarbonyl.

EXPERIMENTAL SECTION

General Remarks. All commercially available reagents were used without further purification. Glassware was dried for 4 h in 140 °C. Solvents used in reactions were distilled over appropriate drying agents prior to use. Solvents used for extraction and purification were distilled prior to use. Reaction temperatures are reported as bath temperature. Thin-layer chromatography (TLC) was performed on TLC silica gel 60 F254. Compounds were visualized with UV light (λ = 254 nm) and/or by immersion in an ethanolic vanillin solution or by immersion in $KMnO_4$ solution followed by heating. Products were purified by flash chromatography on silica gel, 0.04−0.063 mm. Melting points were obtained on a melting point apparatus with open capillary tubes and are uncorrected. IR spectra were measured on a FT-IR spectrometer. UV/vis spectra were recorded with a spectrophotometer. ^{1}H (^{13}C) NMR spectra were recorded at 300 (75) and 500 (125) MHz using $CDCl_3$ or CD_3OD as the solvent. The ^{1}H and ^{13}C chemical shifts were referenced to residual solvent signals at δ H/C 7.26/77.00 ($CDCl_3$) and 3.31/49.1 (CD_3OD) relative to TMS as internal standard. HSQC, HMBC, NOESY, ROESY, HSQMBC, and COSY spectra were recorded on a NMR spectrometer at 500 and 300 MHz. Coupling constants *J* (Hz) were directly taken from the spectra and are not averaged. Splitting patterns are designated as s (singlet), d (doublet), t (triplet), q (quartet), quin (quintet), m (multiplet), and br (broad). 1D and 2D homonuclear NMR spectra were measured with standard pulse sequences. Low-resolution electron impact mass spectra (MS) and exact mass electron impact mass spectra (HRMS) were obtained at 70 eV using a double-focusing sector field mass spectrometer. Intensities are reported as percentages relative to the base peak (I = 100%).

General Procedure. An oven-dried sealed tube was flushed with argon and charged with pivalic acid (122 mg, 1.2 mmol), Cs_2CO_3 (651 mg, 1.5 mmol), a 1,2-dihaloarene **1** (1 mmol), a 1,3-diketone **2** (1.5 mmol), and CuI (19 mg, 0.1 mmol). The tube was evacuated and backfilled with argon two times, and dry DMF (2 mL) was added. The reaction mixture was stirred at 130 °C until the 1,2-dihaloarene **1** was

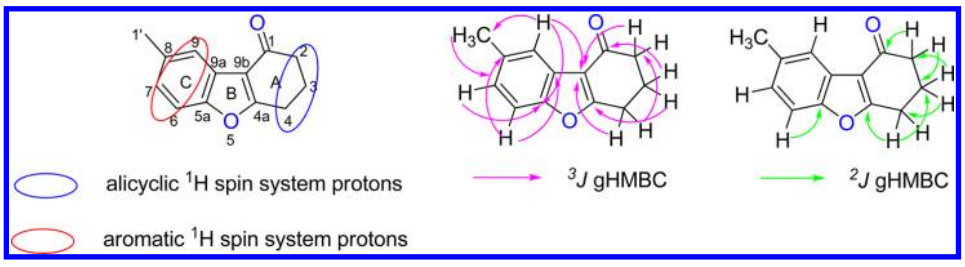
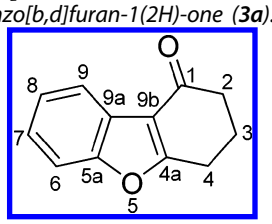


Figure 2. ^{1}H spin system and important HMBC correlations (H→C) for **3j**.

dx.doi.org/10.1021/jo3014275 | J. Org. Chem. 2012, 77, 7793−7803

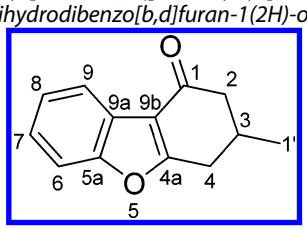
consumed. After being cooled to room temperature, the reaction mixture was partitioned between EtOAc (30 mL) and saturated ammonium chloride (20 mL). The organic layer was isolated, and the aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated in vacuum. The residue was purified by flash chromatography on silica gel to afford the desired product.

*3,4-Dihydrodibenzo[b,d]furan-1(2H)-one (**3a**).*[7,13]



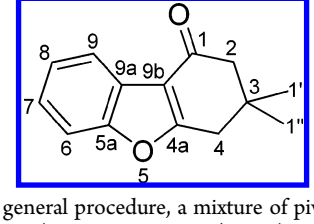
According to the general procedure, a mixture of pivalic acid (122 mg, 1.2 mmol), Cs_2CO_3 (651 mg, 1.5 mmol), **1a** (283 mg, 1 mmol), **2a** (183 mg, 1.5 mmol), and CuI (19 mg, 0.1 mmol) was reacted in dry DMF (2 mL) in a sealed vial at 130 °C for 28 h. Flash chromatography over silica gel (cyclohexane/EtOAc = 8:1) gave **3a** as a pale yellow oil in 75% yield (139 mg, 0.75 mmol): R_f = 0.26 (cyclohexane/EtOAc = 3:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.28 (quin, ^3J (2-H, 3-H) = 6.2 Hz, ^3J (3-H, 4-H) = 6.2 Hz, 2H, 3-H), 2.61 (t, ^3J (2-H, 3-H) = 6.2 Hz, 2H, 2-H), 3.04 (t, ^3J (3-H, 4-H) = 6.2 Hz, 2H, 4-H), 7.28–7.32 (m, 1H, 7-H), 7.31–7.35 (m, 1H, 8-H), 7.45–7.48 (m, 1H, 6-H), 8.04–8.07 (m, 1H, 9-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.5 (C-3), 23.8 (C-4), 37.9 (C-2), 111.0 (C-6), 116.5 (C-9b), 121.8 (C-9), 123.7 (C-9a), 124.4 (C-8), 125.0 (C-7), 154.5 (C-5a), 170.8 (C-4a), 194.8 (C-1); MS (EI, 70 eV) m/z 186 (60) $[M^+]$, 158 (80) $[186 - C_2H_4]^+$, 130 (56) $[158 - CO]^+$.

*3-Methyl-3,4-dihydrodibenzo[b,d]furan-1(2H)-one (**3b**).*



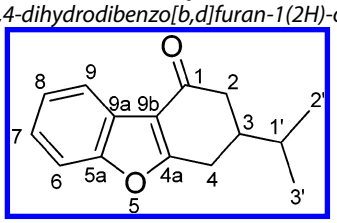
According to the general procedure, a mixture of pivalic acid (122 mg, 1.2 mmol), Cs_2CO_3 (651 mg, 1.5 mmol), **1a** (283 mg, 1 mmol), **2b** (201 mg, 1.5 mmol), and CuI (19 mg, 0.1 mmol) was reacted in dry DMF (2 mL) in a sealed vial at 130 °C for 20 h. Flash chromatography over silica gel (cyclohexane/EtOAc = 8:1) gave **3b** as a white solid in 78% yield (156 mg, 0.78 mmol): mp 96–97 °C; R_f = 0.43 (cyclohexane/EtOAc = 3:1); IR (ATR) $\tilde{\nu}$ 1663 (C═O), 1596, 1449, 1169, 1039, 885, 748, 666 cm^{-1}; UV (MeCN) λ_{max} (log ε) 227 (4.28), 249 (4.02) nm; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.24 (d, ^3J (1′-H, 3-H) = 6.4 Hz, 3H, 1′-H), 2.36 (dd, ^3J (2-Ha, 3-H) = 11.0 Hz, ^2J (2-Ha, 2-Hb) = 15.8 Hz, 1H, 2-Ha), 2.42–2.61 (m, 1H, 3-H), 2.65 (dd, ^3J (2-Hb, 3-H) = 3.6 Hz, ^2J (2-Ha, 2-Hb) = 15.8 Hz, 1H, 2-Hb), 2.71 (dd, ^3J (3-H, 4-Ha) = 9.4 Hz, ^2J (4-Ha, 4-Hb) = 17.2 Hz, 1H, 4-Ha), 3.11 (dd, ^3J (3-H, 4-Hb) = 4.7 Hz, ^2J (4-Ha, 4-Hb) = 17.2 Hz, 1H, 4-Hb), 7.27–7.32 (m, 1H, 7-H), 7.31–7.36 (m, 1H, 8-H), 7.45–7.48 (m, 1H, 6-H), 8.0–8.09 (m, 1H, 9-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.0 (C-1′), 30.6 (C-3), 31.7 (C-4), 46.3 (C-2), 111.0 (C-6), 116.1 (C-9b), 121.6 (C-9), 123.6 (C-9a), 124.4 (C-8), 124.9 (C-7), 154.7 (C-5a), 170.4 (C-4a), 194.3 (C-1); MS (EI, 70 eV) m/z 200 (64) $[M^+]$, 185 (4) $[M - CH_3]^+$, 158 (100) $[185 - C_2H_3]^+$, 130 (52) $[158 - CO]^+$; HRMS (EI, M^+) calcd for $C_{13}H_{12}O_2$ (200.0837), found 200.0827.

*3,3-Dimethyl-3,4-dihydrodibenzo[b,d]furan-1(2H)-one (**3c**).*[13]



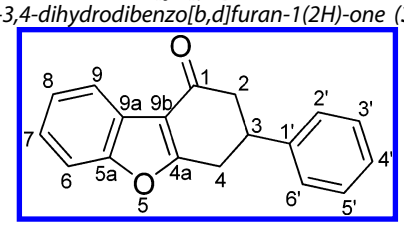
According to the general procedure, a mixture of pivalic acid (122 mg, 1.2 mmol), Cs_2CO_3 (651 mg, 1.5 mmol), **1a** (283 mg, 1 mmol), **2c** (222 mg, 1.5 mmol), and CuI (19 mg, 0.1 mmol) was reacted in dry DMF (2 mL) in a sealed vial at 130 °C for 24 h. Flash chromatography over silica gel (cyclohexane/EtOAc = 10:1) gave **3c** as a yellow solid in 80% yield (172 mg, 0.80 mmol): mp 121–122 °C (lit.[17] mp 120.8–121.1 °C); R_f = 0.50 (cyclohexane/EtOAc = 3:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.20 (s, 6H, 1′-H, 1″-H), 2.49 (s, 2H, 2-H), 2.90 (s, 2H, 4-H), 7.28–7.32 (m, 1H, 7-H), 7.30–7.35 (m, 1H, 8-H), 7.46–7.49 (m, 1H, 6-H), 8.03–8.06 (m, 1H, 9-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.6 (C-1′, C-1″), 35.2 (C-3), 37.7 (C-4), 52.2 (C-2), 111.1 (C-6), 115.3 (C-9b), 121.7 (C-9), 123.6 (C-9a), 124.4 (C-8), 124.8 (C-7), 154.9 (C-5a), 169.9 (C-4a), 194.1 (C-1); MS (EI, 70 eV) m/z 214 (28) $[M^+]$, 199 (52) $[M - CH_3]^+$, 158 (8) $[199 - C_3H_5]^+$.

*3-Isopropyl-3,4-dihydrodibenzo[b,d]furan-1(2H)-one (**3d**).*



According to the general procedure, a mixture of pivalic acid (122 mg, 1.2 mmol), Cs_2CO_3 (651 mg, 1.5 mmol), **1a** (283 mg, 1 mmol), **2d** (248 mg, 1.5 mmol), and CuI (19 mg, 0.1 mol) was reacted in dry DMF (2 mL) in a sealed vial at 130 °C for 24 h. Flash chromatography over silica gel (cyclohexane/EtOAc = 8:1) gave **3d** as a colorless oil in 80% yield (182 mg, 0.80 mmol): R_f = 0.55 (cyclohexane/EtOAc = 3:1); IR (ATR) $\tilde{\nu}$ 1663 (C═O), 1590, 1449, 1171, 1039, 833, 750, 670 cm^{-1}; UV (MeCN) λ_{max} (log ε) 289 (3.61), 265 (3.90), 249 (3.94), 227 (4.18) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.02 (d, ^3J (1′-H, 2′-H) = 6.9 Hz, 3H, 2′-H), 1.02 (d, ^3J (1′-H, 3′-H) = 6.9 Hz, 3H, 3′-H), 1.69–1.96 (m, 1H, 1′-H), 2.13–2.29 (m, 1H, 3-H), 2.40 (dd, ^3J (2-Ha, 3-H) = 1.3 Hz, ^2J (2-Ha, 2-Hb) = 15.9 Hz, 1H, 2-Ha), 2.67 (dd, ^3J (2-Hb, 3-H) = 3.7 Hz, ^2J (2-Ha, 3-Hb) = 16.1 Hz, 1H, 2-Hb), 2.78 (dd, ^3J (3-H, 4-Ha) = 10.7 Hz, ^2J (4-Ha, 4-Hb) = 17.3 Hz, 1H, 4-Ha), 3.07 (dd, ^3J (3-H, 4-Hb) = 5.0 Hz, ^2J (4-Ha, 4-Hb) = 17.5 Hz, 1H, 4-Hb), 7.27–7.32 (m, 1H, 7-H), 7.31–7.36 (m, 1H, 8-H), 7.42–7.51 (m, 1H, 6-H), 7.99–8.08 (m, 1H, 9-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.62 (C-3′), 19.85 (C-2′), 27.4 (C-4), 32.0 (C-1′), 42.05 (C-3), 42.16 (C-2), 111.1 (C-6), 116.3 (C-9b), 121.7 (C-9), 123.6 (C-9a), 124.4 (C-8), 124.9 (C-7), 154.8 (C-5a), 171.1 (C-4a), 194.7 (C-1); MS (EI, 70 eV) m/z 228 (88) $[M^+]$, 213 (4) $[M - CH_3]^+$, 185 (10) $[213 - C_2H_4]^+$, 158 (100) $[185 - C_2H_3]^+$, 130 (38) $[158 - CO]^+$; HRMS (EI; M^+) calcd for $C_{15}H_{16}O_2$ (228.1150), found 228.1146.

*3-Phenyl-3,4-dihydrodibenzo[b,d]furan-1(2H)-one (**3e**).*



According to the general procedure, a mixture of pivalic acid (122 mg, 1.2 mmol), Cs_2CO_3 (651 mg, 1.5 mmol), **1a** (283 mg, 1 mmol), **2e** (282 mg, 1.5 mmol), and CuI (19 mg, 0.1 mmol) was reacted in dry DMF (2 mL) in a sealed vial at 130 °C for 24 h. Flash chromatography over silica gel (cyclohexane/EtOAc = 10:1) gave **3e** as a white solid in 62% yield (162 mg, 0.62 mmol): mp 156–157 °C; R_f = 0.53 (cyclohexane/EtOAc = 3:1); IR (ATR) $\tilde{\nu}$ 1652 (C═O), 1587, 1482, 1402, 1168, 1043, 833, 759, 740, 694, 668 cm^{-1}; UV (MeCN) λ_{max} (log ε) 265 (3.85), 249 (3.96), 227 (4.34) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.83–2.98 (m, 2H, 2-H), 3.24 (dd, ^3J (3-H, 4-Ha) = 10.6 Hz, ^2J (4-Ha, 4-Hb) = 17.6 Hz, 1H, 4-Ha), 3.34 (dd, ^3J (3-H, 4-Hb) = 5.4 Hz, ^2J (4-Ha, 4-Hb) = 17.6 Hz, 1H, 4-Hb), 3.62–3.75 (m, 1H, 3-H), 7.27–7.37 (m, 2H, 2′-H, 6′-H), 7.30–7.40 (m, 3H, 7-H, 8-H, 4′-H), 7.35–7.44 (m, 2H, 3′-H, 5′-H), 7.45–7.53 (m, 1H, 6-H), 8.05–8.13 (m, 1H, 9-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.6 (C-4), 41.2 (C-3), 45.2 (C-2), 111.2 (C-6), 116.5 (C-9b), 121.8 (C-9), 123.5 (C-9a), 124.6 (C-8), 125.1 (C-7), 126.8 (C-2′), 127.3 (C-4′), 128.9 (C-3′), 142.2 (C-1′), 154.9 (C-5a), 169.9 (C-4a), 193.3 (C-1); MS

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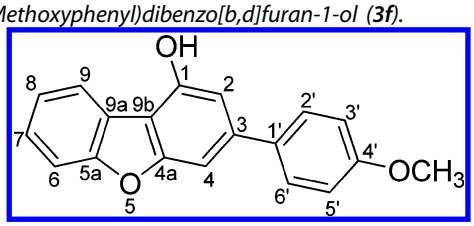
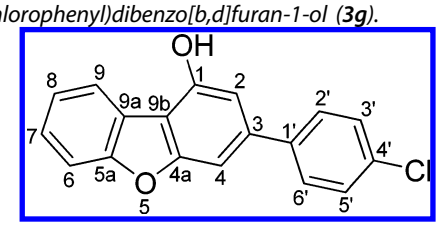
(EI, 70 eV) m/z 262 (56) [M^+], 158 (100) [$M - C_8H_8]^+$, 130 (32) [$158 - CO]^+$; HRMS (EI; M^+) calcd for $C_{18}H_{14}O_2$ (262.0994), found 262.0996.

*3-(4-Methoxyphenyl)dibenzo[b,d]furan-1-ol (**3f**).*



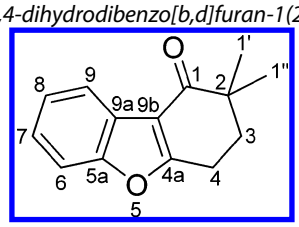
According to the general procedure, a mixture of pivalic acid (122 mg, 1.2 mmol), Cs_2CO_3 (651 mg, 1.5 mmol), **1a** (283 mg, 1 mmol), **2f** (327 mg, 1.5 mmol), and CuI (19 mg, 0.1 mmol) was reacted in dry DMF (2 mL) in a sealed vial at 130 °C for 26 h. Flash chromatography over silica gel (cyclohexane/EtOAc = 6:1) gave **3f** as a white solid in 64% yield (187 mg, 0.64 mmol): mp 181−182 °C; R_f = 0.32 (cyclohexane/EtOAc = 3:1); IR (ATR) $\tilde{\nu}$ 3396 (O−H), 1601, 1517, 1426, 1406, 1227, 1054, 1018, 850, 816, 807, 743, 716 cm^{-1}; UV (MeCN) λ_{max} (log ε) 292 (4.38), 225 (4.36) nm; ^{1}H NMR (300 MHz, CD_3OD) δ 3.02 (s, 3H, OCH_3), 6.96 (d, ^4J (2-H, 4-H) = 1.0 Hz, 1H; 2-H), 6.98−7.02 (m, 2H, 3′-H, 5′-H), 7.22 (d, ^4J (2-H, 4-H) = 1.0 Hz, 1H, 4-H), 7.30 (ddd, ^4J (6-H, 8-H) = 1.2 Hz, ^3J (7-H, 8-H) = 7.3 Hz, ^3J (8-H, 9-H)= 7.3 Hz, 1H, 8-H), 7.38 (ddd, ^4J (7-H, 9-H) = 1.3 Hz, ^3J (6-H, 7-H) = 7.5 Hz, ^3J (7-H, 8-H) = 7.5 Hz, 1H, 7-H), 7.50 (bd ^3J (6-H, 7-H) = 7.4 Hz, 1H, 6-H), 7.57−7.60 (m, 2H, 2′-H, 6′-H), 8.08 (dd, ^4J (7-H, 9-H) = 1.5 Hz, ^3J (8-H, 9-H) = 7.6 Hz, 1H, 9-H); ^{13}C NMR (75 MHz, CD_3OD) δ 55.9 (OCH_3), 101.8 (C-4), 108.3 (C-2), 111.8 (C-6), 112.5 (C-9b), 115.4 (C-3′), 123.6 (C-9), 123.9 (C-8), 125.1 (C-9a), 127.0 (C-7), 129.3 (C-2′), 135.0 (C-1′), 143.0 (C-3), 155.1 (C-1), 157.3 (C-5a), 159.8 (C-4a), 161.0 (C-4′); MS (EI, 70 eV) m/z 290 (100) [M^+], 275 (44) [$M - CH_3]^+$, 247 (20) [$275 - CO]^+$, 218 (6), 189 (8), 145 (10); HRMS (EI, M^+) calcd for $C_{19}H_{14}O_3$ (290.0943), found 290.0933.

*3-(4-Chlorophenyl)dibenzo[b,d]furan-1-ol (**3g**).*



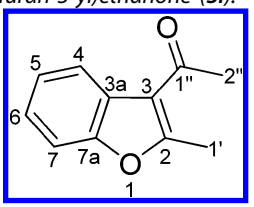
According to the general procedure, a mixture of pivalic acid (122 mg,1.2 mmol), Cs_2CO_3 (651 mg, 1.5 mmol), **1a** (283 mg, 1 mmol), **2g** (334 mg, 1.5 mmol), and CuI (19 mg, 0.1 mmol) was reacted in dry DMF (2 mL) in a sealed vial at 130 °C for 26 h. Flash chromatography over silica gel (cyclohexane/EtOAc = 6:1) gave **3g** as an orange solid in 61% yield (180 mg, 0.61 mmol): mp 165−166 °C; R_f = 0.45 (cyclohexane/EtOAc = 3:1); IR (ATR) $\tilde{\nu}$ 3410 (O−H), 1601, 1483, 1453, 1424, 1227, 1188, 1048, 847, 821, 750, 724, 685 cm^{-1}; UV (MeCN) λ_{max} (log ε) 291 (4.39), 232 (4.37), 225 (4.38) nm; ^{1}H NMR (300 MHz, CD_3OD) δ 6.96 (d, ^4J (2-H, 4-H) = 0.9 Hz, 1H, 2-H), 7.27 (d, ^4J (2-H, 4-H) = 0.9 Hz, 1H, 4-H), 7.31 (ddd, ^4J (6-H, 8-H) = 1.2 Hz, ^3J (7-H, 8-H) = 7.4 Hz, ^3J (8-H, 9-H) = 7.4 Hz, 1H, 8-H), 7.40 (ddd, ^4J (7-H, 9-H) = 1.7 Hz, ^3J (6-H, 7-H) = 8.0 Hz, ^3J (7-H, 8-H) = 8.0 Hz, 1H, 7-H), 7.40−7.45 (m, 2H, 3′-H, 5′-H), 7.51 (bd, ^3J (6-H, 7-H) = 8.1 Hz, 1H, 6-H), 7.60−7.65 (m, 2H, 2′-H, 6′-H), 8.09 (dd, ^4J (7-H, 9-H) = 1.6 Hz, ^3J (8-H, 9-H) = 7.7 Hz, 1H, 9-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 102.3 (C-2), 108.5 (C-4), 111.9 (C-6), 113.4 (C-9b), 123.8 (C-9), 124.0 (C-8), 124.9 (C-9a), 127.3 (C-7), 129.8 (C-2′), 130.0 (C-3′), 134.6 (C-3), 141.3 (C-1′), 141.7 (C-4′), 155.2 (C-1), 157.4 (C-5a), 159.7 (C-4a); MS (EI, 70 eV) m/z 294 (100) [M^+], 265 (8), 231 (10), 202 (12), 147 (8); HRMS (EI; M^+) calcd for $C_{18}H_{11}ClO_2$ (294.0448) found, 294.0427.

*4,4-Dimethyl-3,4-dihydrodibenzo[b,d]furan-1(2H)-one (**3h**).*



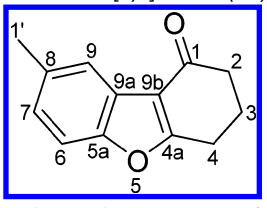
According to the general procedure, a mixture of pivalic acid (122 mg, 1.2 mmol), Cs_2CO_3 (651 mg, 1.5 mmol), **1a** (283 mg, 1 mmol), **2h** (222 mg, 1.5 mmol), and CuI (19 mg, 0.1 mmol) was reacted in dry DMF (2 mL) in a sealed vial at 130 °C for 24 h. Flash chromatography over silica gel (cyclohexane/EtOAc = 10:1) gave **3h** as a colorless oil in 78% yield (167 mg, 0.78 mmol): R_f = 0.57 (cyclohexane/EtOAc = 3:1); IR (ATR) $\tilde{\nu}$ 1666 (C═O), 1588, 1478, 1405, 1172, 1040, 749, 671 cm^{-1}; UV (MeCN) λ_{max} (log ε) 282 (3.81), 260 (3.98), 249 (4.07), 227 (4.36) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24 (s, 6H, 1′-H, 1″-H), 2.10 (brt, ^3J (3-H, 4-H) = 6.2 Hz, 2H, 3-H), 3.05 (brt, ^3J (3-H, 4-H) = 6.3 Hz, 2H, 4-H), 7.30−7.35 (m, 1H, 7-H), 7.34−7.39 (partially overlapped, 1H, 8-H); 7.45−7.54 (m, 1H, 6-H), 8.05−8.14 (m, 1H, 9-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.4 (C-4), 24.1 (C-1′), 36.3 (C-3), 42.2 (C-2), 111.0 (C-6), 114.7 (C-9b), 121.8 (C-9), 124.3 (C-8), 124.3 (the chemical shift was overlapped indirectly by HMBC, C-9a); 124.8 (C-7), 154.9 (C-5a), 169.0 (C-4a), 199.7 (C-1); MS (EI, 70 eV) m/z 214 (16) [M^+], 199 (6) [$M - CH_3]^+$,158 (36) [$199 - C_3H_5]^+$, 130 (16) [$158 - CO]^+$, 102 (8); HRMS (EI, M^+) calcd for $C_{14}H_{14}O_2$ (214.0994), found 214.0973.

*1-(2-Methylbenzofuran-3-yl)ethanone (**3i**).*[7,13]



According to the general procedure, a mixture of pivalic acid (122 mg, 1.2 mmol), Cs_2CO_3 (651 mg, 1.5 mmol), **1a** (283 mg, 1 mmol), **2i** (150 mg, 1.5 mmol), and CuI (19 mg, 0.1 mmol) was reacted in dry DMF (2 mL) in a sealed vial at 130 °C for 22 h. Flash chromatography over silica gel (dichloromethane/EtOAc = 99:1) gave **3i** as a pale yellow oil in 83% yield (144 mg, 0.83 mmol): R_f = 0.45 (cyclohexane/EtOAc= 3:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.65 (s, 3H, 1′-H), 2.78 (s, 3H, 2″-H), 7.28−7.32 (m, 1H, 6-H), 7.31−7.35 (m, 1H, 5-H), 7.44−7.47 (m, 1H, 7-H), 7.93−7.96 (m, 1H, 4-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.4 (C-1′), 31.2 (C-2″), 111.0 (C-7), 117.6 (C-3), 121.3 (C-4), 124.0 (C-3a), 124.4(C-5), 126.0 (C-6), 153.5 (C-7a), 162.8 (C-2), 194.3 (C-1″); MS (EI, 70 eV) m/z 174 (20) [M^+], 159 (42) [$M - CH_3]^+$,103 (4).

*8-Methyl-3,4-dihydrodibenzo[b,d]furan-1(2H)-one (**3j**).*



According to the general procedure, a mixture of pivalic acid (122 mg, 1.2 mmol), Cs_2CO_3 (651 mg, 1.5 mmol), **1b** (297 mg, 1 mmol), **2a** (183 mg, 1.5 mmol), and CuI (19 mg, 0.1 mmol) was reacted in dry DMF (2 mL) in a sealed vial at 130 °C for 23 h. Flash chromatography over silica gel (dichloromethane/EtOAc = 20:1) gave **3j** as a white solid in 77% yield (154 mg, 0.77 mmol): mp 86−87 °C; R_f = 0.36 (cyclohexane/EtOAc = 3:1); IR (ATR) $\tilde{\nu}$ 1663 (C═O), 1586, 1456, 1395, 1175, 1056, 1002, 883, 814, 801, 778 cm^{-1}; UV (MeCN) λ_{max} (log ε) 287 (3.61), 252 (3.96), 232 (4.26) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.45 (s, 3H, 1′-H), 2.27 (quin, ^3J (2-H, 3-H) = 6.2 Hz, ^3J (3-H, 4-H) = 6.2 Hz, 2H, 3-H), 2.60 (brt, ^3J (2-H, 3-H) = 6.2 Hz, 2H, 2-H), 3.02 (brt, ^3J (3-H, 4-H) = 6.3 Hz, 2H, 4-H), 7.11 (dd, ^4J (7-H,

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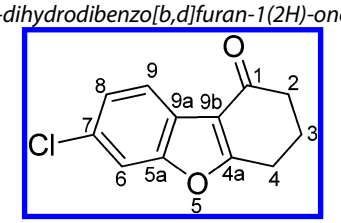
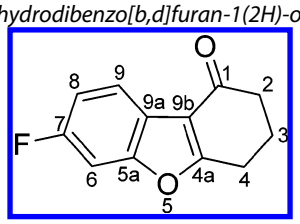
9-H) = 1.0 Hz, ^3J (6-H, 7-H) = 8.4 Hz, 1H, 7-H), 7.34 (d, ^3J (6-H, 7-H) = 8.4 Hz, 1H, 6-H), 7.86 (brs, 1H, 9-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.3 (C-1′), 22.5 (C-3), 23.9 (C-4), 37.9 (C-2), 110.5 (C-6), 116.3 (C-9b), 121.7 (C-9), 123.7 (C-9a), 126.0 (C-7), 134.2 (C-8), 153.0 (C-5a), 170.9 (C-4a), 194.9 (C-1); MS (EI, 70 eV) m/z 200 (98) [M^+], 172 (100) [200 − C_2H_4]$^+$, 144 (62) [172 − CO]$^+$, 115 (20); HRMS (EI; M^+) calcd for $C_{13}H_{12}O_2$ (200.0837), found 200.0854.

*7-Chloro-3,4-dihydrodibenzo[b,d]furan-1(2H)-one (**3k**).*



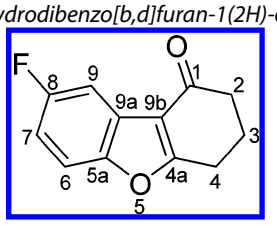
According to the general procedure, a mixture of pivalic acid (122 mg, 1.2 mmol), Cs_2CO_3 (651 mg, 1.5 mmol), **1c** (317 mg, 1 mmol), **2a** (183 mg, 1.5 mmol), and CuI (19 mg, 0.1 mmol) was reacted in dry DMF (2 mL) in a sealed vial at 130 °C for 20 h. Flash chromatography over silica gel (dichloromethane/EtOAc = 20:1) gave **3k** as a colorless oil in 71% yield (157 mg, 0.71 mmol): R_f = 0.29 (cyclohexane/EtOAc = 3:1); IR (ATR) $\tilde{\nu}$ 1652 (C═O), 1582, 1472, 1404, 1169, 1053, 1006, 896, 829, 722 cm^{-1}; UV (MeCN) λ_{max} (log ε) 289 (3.63), 281 (3.75), 253 (4.17), 227 (4.34) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.28 (quin, ^3J (2-H, 3-H) = 6.3 Hz, ^3J (3-H, 4-H) = 6.3 Hz, 2H, 3-H), 2.61 (brt, ^3J (2-H, 3-H) = 6.6 Hz, 2H, 2-H), 3.03 (brt, ^3J (3-H, 4-H) = 6.2 Hz, 2H, 4-H), 7.31 (dd, ^4J (6-H, 8-H) = 1.7 Hz, ^3J (8-H, 9-H) = 8.3 Hz, 1H, 8-H), 7.48 (d, ^4J (6-H, 8-H) = 1.7 Hz, 1H, 6-H), 7.95 (d, ^3J (8-H, 9-H) = 8.4 Hz, 1H, 9-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.4 (C-3), 23.8 (C-4), 37.8 (C-2), 111.8 (C-6), 116.3 (C-9b), 122.3 (C-9), 122.4 (C-9a), 125.1 (C-8), 130.8 (C-7), 154.5 (C-5a), 171.3 (C-4a), 194.4 (C-1); MS (EI, 70 eV) m/z 220 (82) [M^+], 192 (100) [M − C_2H_4]$^+$, 164 (68) [192 − CO]$^+$, 136 (38); HRMS (EI; M^+) calcd for $C_{12}H_9ClO_2$ (220.0291), found 220.0275.

*7-Fluoro-3,4-dihydrodibenzo[b,d]furan-1(2H)-one (**3l**).*



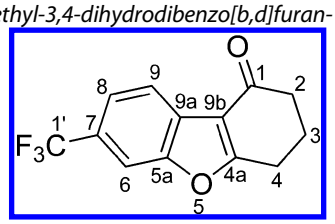
According to the general procedure, a mixture of pivalic acid (122 mg, 1.2 mmol), Cs_2CO_3 (651 mg, 1.5 mmol), **1d** (300 mg, 1 mmol), **2a** (183 mg, 1.5 mmol), and CuI (19 mg, 0.1 mmol) was reacted in dry DMF (2 mL) in a sealed vial at 130 °C for 20 h. Flash chromatography over silica gel (dichloromethane/EtOAc = 20:1) gave **3l** as a colorless oil in 66% yield (136 mg, 0.66 mmol): R_f = 0.28 (cyclohexane/EtOAc = 3:1); IR (ATR) $\tilde{\nu}$ 1666 (C═O), 1595, 1488, 1407, 1172, 1094, 1007, 936, 865, 818, 787, 769 cm^{-1}; UV (MeCN) λ_{max} (log ε) 285 (3.85), 276 (3.90), 260 nm (3.93); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.28 (quin, ^3J (2-H, 3-H) = 6.2 Hz, ^3J (3-H, 4-H) = 6.2 Hz, 2H, 3-H), 2.60 (t, ^3J (2-H, 3-H) = 6.0 Hz, 2H, 2-H), 3.03 (t, ^3J (3-H, 4-H) = 6.2 Hz, 2H, 4-H), 7.08 (ddd, ^4J (6-H, 8-H) = 2.2 Hz, ^3J (8-H, 9-H) = 9.2 Hz, ^3J (F, 8-H) = 9.2 Hz, 1H, 8-H), 7.19 (dd, ^4J (6-H, 8-H) = 2.2 Hz, ^3J (F, 6-H) = 8.6, 1H, 6-H), 7.97 (dd, ^4J (F, 9-H) = 5.6 Hz, ^3J (8-H, 9-H) = 8.7, 1H, 9-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.5 (C-3), 23.8 (C-4), 37.7 (C-2), 99.2 (d, ^2J (^{19}F, ^{13}C) = 27.0 Hz, C-6), 112.5 (d, ^2J (^{19}F, ^{13}C) = 23.5 Hz, C-8), 116.3 (C-9b), 120.0 (d, ^4J (^{19}F, ^{13}C) = 1.9 Hz, C-9a), 122.2 (d, ^3J (^{19}F, ^{13}C) = 9.8 Hz, C-9), 154.5 (d, ^3J (^{19}F, ^{13}C) = 12.9 Hz, C-5a), 161.0 (d, ^1J (^{19}F, ^{13}C) = 243.4 Hz, C-7), 171.2 (d, ^5J (^{19}F, ^{13}C) = 3.0, C-4a), 194.5 (C-1); MS (EI, 70 eV) m/z 204 (64) [M^+], 176 (90) [M − C_2H_4]$^+$, 148 (72) [176 − CO]$^+$, 120 (78); HRMS (EI; M^+) calcd for $C_{12}H_9FO_2$ (204.0587), found 204.0606.

*8-Fluoro-3,4-dihydrodibenzo[b,d]furan-1(2H)-one (**3m**).*



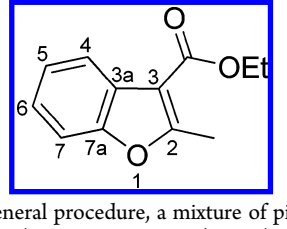
According to the general procedure, a mixture of pivalic acid (122 mg, 1.2 mmol), Cs_2CO_3 (651 mg, 1.5 mmol), **1e** (300 mg, 1 mmol), **2a** (183 mg, 1.5 mmol), and CuI (19 mg, 0.1 mmol) was reacted in dry DMF (2 mL) in a sealed vial at 130 °C for 20 h. Flash chromatography over silica gel (dichloromethane/EtOAc = 20:1) gave **3m** as a colorless oil in 64% yield (130 mg, 0.64 mmol): R_f = 0.30 (cyclohexane/EtOAc = 3:1); IR (ATR) $\tilde{\nu}$ 1658 (C═O), 1596, 1582, 1449, 1395, 1165, 1133, 1004, 869, 804, 784, 681 cm^{-1}; UV (MeCN) λ_{max} (log ε) 285 (3.49), 252 (3.88), 228 (4.20); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.28 (quin, ^3J (2-H, 3-H) = 6.2 Hz, ^3J (3-H, 4-H) = 6.2 Hz, 2H, 3-H), 2.61 (t, ^3J (2-H, 3-H) = 6.2 Hz, 2H, 2-H), 3.04 (t, ^3J (3-H, 4-H) = 6.3 Hz, 2H, 4-H), 7.02 (ddd, ^4J (7-H, 9-H) = 2.6 Hz, ^3J (6-H, 7-H) = 9.1 Hz, ^3J (F,7-H) = 9.1 Hz, 1H, 7-H), 7.40 (dd, ^3J (6-H, 7-H) = 8.9 Hz, ^4J (F, 6-H) = 3.9, 1H, 6-H), 7.72 (dd, ^4J (7-H, 9-H) = 2.7 Hz, ^3J (F, 9-H) = 8.1, 1H, 9-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.4 (C-3), 23.9 (C-4), 37.7 (C-2), 107.8 (d, ^2J (^{19}F, ^{13}C) = 26.2 Hz, C-9), 111.7 (d, ^2J (^{19}F, ^{13}C) = 9.7 Hz, C-6), 112.5 (d, ^3J (^{19}F, ^{13}C) = 26.0 Hz, C-7), 116.7 (C-9b), 124.7 (d, ^3J (^{19}F, ^{13}C) = 11.5 Hz, C-9a), 150.7 (d, ^4J (^{19}F, ^{13}C) = 1.0 Hz, C-5a), 160.2 (d, ^1J (^{19}F, ^{13}C) = 240.6 Hz, C-8), 172.2 (C-4a), 194.4 (C-1); MS (EI, 70 eV) m/z 204.2 (62) [M^+], 176 (90) [M − C_2H_4]$^+$, 148 (74) [176 − CO]$^+$, 120 (78); HRMS (EI; M^+) calcd for $C_{12}H_9FO_2$ (204.0587), found 204.0578.

*7-Trifluoromethyl-3,4-dihydrodibenzo[b,d]furan-1(2H)-one (**3n**).*



According to the general procedure, a mixture of pivalic acid (122 mg, 1.2 mmol), Cs_2CO_3 (651 mg, 1.5 mmol), **1f** (351 mg, 1 mmol), **2a** (183 mg, 1.5 mmol), and CuI (19 mg, 0.1 mmol) was reacted in dry DMF (2 mL) in a sealed vial at 100 °C for 28 h. Flash chromatography over silica gel (dichloromethane/EtOAc = 20:1) gave **3n** as a colorless oil in 47% yield (119 mg, 0.47 mmol): R_f = 0.27 (cyclohexane/EtOAc = 3:1); IR (ATR) $\tilde{\nu}$ 1673 (C═O), 1587, 1408, 1322, 1161, 1112, 1004, 904, 876, 826, 689 cm^{-1}; UV (MeCN) λ_{max} (log ε) 281 (3.58), 252 (4.28) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.31 (quin, ^3J (2-H, 3-H) = 6.3 Hz, ^3J (3-H, 4-H) = 6.3 Hz, 2H, 3-H), 2.64 (t, ^3J (2-H, 3-H) = 6.2 Hz, 2H, 2-H), 3.09 (t, ^3J (3-H, 4-H) = 6.3 Hz, 2H, 4-H), 7.61 (brd, ^3J (8-H, 9-H) = 8.4 Hz, 1H, 8-H), 7.74 (brs, 1H, 6-H), 8.15 (d, ^3J (8-H, 9-H) = 8.1, 1H, 9-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.3 (C-3), 23.9 (C-4), 37.8 (C-2), 108.7 (d, ^3J (^{19}F, ^{13}C) = 4.2 Hz, C-6), 116.3 (C-9b), 121.6 (d, ^3J (^{19}F, ^{13}C) = 3.6 Hz, C-8), 122.2 (brs, C-9), 124.5 (q, ^1J (^{19}F, ^{13}C) = 270.6 Hz, C-1′), 126.8 (C-9a), 127.3 (d, ^2J (^{19}F, ^{13}C) = 32.6 Hz, C-7), 153.7 (C-5a), 172.9 (C-4a), 194.3 (C-1); MS (EI, 70 eV) m/z 254 (60) [M^+], 235 (28) [M − F]$^+$, 226 (100), 204 (12), 198 (46), 176 (10), 170 (40), 138 (8); HRMS (EI; M^+) calcd for $C_{13}H_9F_3O_2$ (254.0555), found 254.0558.

*Ethyl 2-Methylbenzofuran-3-carboxylate (**6**).*[7,13]



According to the general procedure, a mixture of pivalic acid (122 mg, 1.2 mmol), Cs_2CO_3 (651 mg, 1.5 mmol), **1a** (283 mg, 1 mmol), **5**

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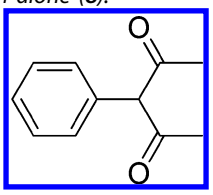
(195 mg, 1.5 mmol), and CuI (19 mg, 0.1 mmol) was reacted in dry DMF (2 mL) in a sealed vial at 130 °C for 24 h. Flash chromatography over silica gel (cyclohexane/EtOAc = 15:1) gave **6** as a brown oil in 63% yield (129 mg, 0.63 mmol): R_f = 0.53 (cyclohexane/EtOAc = 5:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.45 (t, ^3J = 7.3, 3H, CH_2CH_3), 2.78 (s, 3H, 2-CH_3), 4.42 (q, ^3J = 7.3, 2H, CH_2CH_3), 7.25−7.32 (m, 2H), 7.42−7.45 (m, 1H), 7.94−7.98 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.4, 60.2, 109.0, 110.7, 121.7, 123.7, 124.2, 126.2, 153.6, 163.6, 164.5.

*3-Phenylpentane-2,4-dione (**8**).*[20f]*



According to the general procedure, a mixture of pivalic acid (122 mg, 1.2 mmol), Cs_2CO_3 (651 mg, 1.5 mmol), **7a** (204 mg, 1 mmol), **2i** (150 mg, 1.5 mmol), and CuI (19 mg, 0.1 mmol) was reacted in dry DMF (2 mL) in a sealed vial at 130 °C for 3 h. Flash chromatography over silica gel (cyclohexane/EtOAc = 20:1) gave **8** as a colorless oil in 61% yield (107 mg, 0.61 mmol): R_f = 0.58 (cyclohexane/EtOAc = 5:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.89 (s, 6H), 7.16−7.20 (m, 2H), 7.32−7.41 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.1, 115.2, 127.5, 128.8, 131.1, 136.9, 190.9.

■ ASSOCIATED CONTENT

Supporting Information

Copies of NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(25) CCDC-867350 (**3j**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre viawww.ccdc.cam.ac.uk/data_request/cif.

NOTE ADDED AFTER ASAP PUBLICATION

The version published ASAP September 4, 2012 contained errors. A correction was made to Figure 1 and the General Remarks and the paper reposted September 10, 2012.