Synthesis of Phthalide Derivatives Using Nickel-Catalyzed Cyclization of *o*-Haloesters with Aldehydes

Dinesh Kumar Rayabarapu, Hong-Tai Chang, and Chien-Hong Cheng*[a]

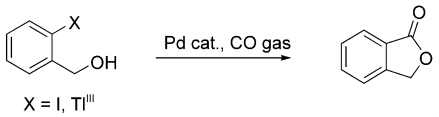
Abstract: The reaction of *o*-bromobenzoate (**1b**) with benzaldehyde (**2a**) in the presence of [$NiBr_2$(dppe)] (dppe = 1,2-bis(diphenylphosphino)ethane) and zinc powder in THF (24 hours, reflux temperature), afforded 3-phenyl-3*H*-isobenzofuran-1-one (**3a**) in an 86% yield. Similarly, *o*-iodobenzoate reacts with **2a** to give **3a**, but in a lower yield (50%). A series of substituted aromatic and aliphatic aldehydes (**2b**, 4-MeC_6H_4CHO; **2c**, 4-$MeOC_6H_4CHO$; **2d**, 3-$MeOC_6H_4CHO$; **2e**, 2-$MeOC_6H_4$-CHO; **2f**, 4-CNC_6H_4CHO; **2g**, 4-$(Me)_3$-CC_6H_4CHO; **2h**, 4-$C_6H_5C_6H_4CHO$; **2i**, 4-ClC_6H_4CHO; **2j**, 4-$CF_3C_6H_4CHO$; **2k**, $CH_3(CH_2)_5CHO$; **2l**, $CH_3(CH_2)_2$-CHO) also underwent cyclization with *o*-bromobenzoate (**1b**) producing the corresponding phthalide derivatives in moderate to excellent yields and with high chemoselectivity. Like **1b**, methyl 2-bromo-4,5-dimethoxybenzoate (**1c**) reacts with tolualdehyde (**2b**) to give the corresponding substituted phthalide **3m** in a 71% yield. The methodology can be further applied to the synthesis of six-membered lactones. The reaction of methyl 2-(2-bromophenyl)acetate (**1d**) with benzaldehyde under similar reaction conditions afforded six-membered lactone **3o** in a 68% yield. A possible catalytic mechanism for this cyclization is also proposed.

Keywords: chemoselectivity · cyclization · heterogeneous catalysis · natural products · nickel

Introduction

Phthalides (isobenzofuranones) are five-membered lactones found in plants. These species possess several important properties, such as fungicidal,[1,2] bactericidal,[2] herbicidal,[2] and analgesic activities.[3] In addition, phthalide derivatives are useful in the treatment of circulatory and heart-related diseases.[4] In spite of their numerous valuable functions, there are only a few efficient metal-mediated reactions known for the synthesis of phthalides.[5–9]

Cowell and Stille reported a cyclocarbonylation[10] of *o*-iodobenzyl alcohols catalyzed by palladium complexes,[5] whereas Larock et al. reported a two-step process involving an *ortho*-thallation of *o*-iodobenzyl alcohols and a palladium-catalyzed cyclocarbonylation of the thallated intermediate (Scheme 1).[6] A palladium-catalyzed carbonylative cyclization of *o*-bromobenzaldehyde in the presence of nucleophiles at very high CO pressure to give phthalide derivatives was also reported.[7] In all these reactions, CO gas was employed as a one-carbon source. Recently, the use of *ortho*-halobenzenes as reagents for the synthesis of five-, six-, and seven-membered carbocycles[11,12] or heterocycles[13] catalyzed by metal complexes has attracted great attention. Our interest in the nickel-catalyzed[14] cyclization reactions led us to investigate the reaction of *o*-halobenzoates with aldehydes in the presence of nickel complexes. Herein, we wish to report a novel, highly chemoselective cyclization of *o*-halobenzoates with aldehydes catalyzed by nickel complexes to afford phthalides. This new cyclization reaction provides a convenient method for the synthesis of various substituted phthalides in a one-pot reaction, with good to excellent yields from easily available starting materials.



Scheme 1. Palladium-catalyzed cyclocarbonylation reaction.

Results and Discussion

The reaction of 2-iodobenzoate (**1a**) with benzaldehyde (**2a**) in THF in the presence of [$NiBr_2$(dppe)] (dppe: bis(di-

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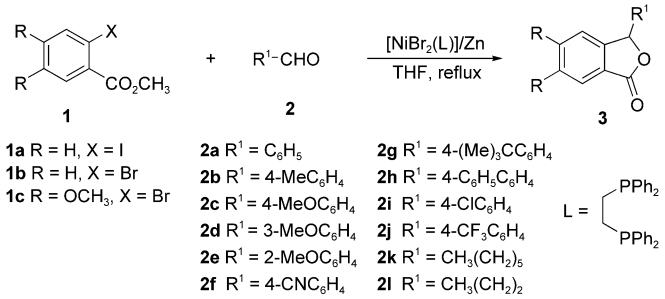
phenylphosphino)ethane) and zinc powder (24 hours, reflux temperature), afforded substituted phthalide **3a** in a 50% yield (Scheme 2 and Table 2 later). Under similar conditions, the reaction of 2-bromobenzoate (**1b**) with **2a** also gave **3a**, but in a much higher yield (86%). Product **3a** was fully



Scheme 2. Nickel-catalyzed cyclization reaction to produce phthalides.

characterized by its spectral data. A common byproduct is (*o*-PhCOOMe)$_2$, from the reductive homocoupling of **1a** or **1b**. The presence of this byproduct is much lower for bromobenzoate **1b** than for the iodo analogue **1a**.

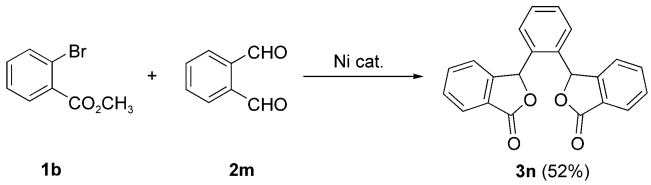
To understand the nature of the present catalytic reaction, the effects of catalyst and solvent on the reaction of **1b** with **2a** were examined, and the results are summarized in Table 1. Nickel complexes with monodentate phosphine ligands, such as [$NiCl_2(PPh_3)_2$], [$NiBr_2(PPh_3)_2$], and [$NiBr_2(PPh_2Me)_2$], afforded a trace of **3a**. No product was observed when [$NiBr_2$(bipy)] (bipy = 2,2′-bipyridine) was used. Complexes containing bidentate phosphine ligands, such as [$NiBr_2$(dppm)], [$NiBr_2$(dppp)], [$NiBr_2$(dppb)], [$NiCl_2$(dppe)], and [NiI_2(dppe)], afforded **3a** in 72, 79, 58, 67, and 71% yields, respectively. [$NiBr_2$(dppe)] appears to be the best catalyst for this cyclization reaction, affording **3a** in an 86% yield. The catalytic reaction also depends greatly on the solvent employed: no reaction occurred in CH_2Cl_2 and both diethyl ether and DMF afforded only a trace of product, whereas, CH_3CN, toluene, dioxane, and ethyl acetate afforded **3a** in moderate yields. THF was found to be the solvent of choice when using [$NiBr_2$(dppe)] as the catalyst. Surprisingly, palladium complexes appear be totally ineffective for this cylization. No product was observed for the reaction of **1a**/**1b** with **2a** in the presence of [$Pd(dba)_2$]/Zn (dba = *trans*,*trans*-dibenzylideneacetone) or [$PdCl_2$(dppe)]/Zn under similar reaction conditions.

Table 1. Effects of ligands and solvent on the cyclization reaction of *o*-bromobenzoate (**1b**) with benzaldehyde (**2a**).[a]

Entry	Catalyst	Solvent	Yield [%][b]
1	–	THF	0
2	[$NiCl_2(PPh_3)_2$]	THF	trace
3	[$NiBr_2(PPh_3)_2$]	THF	trace
4	[$NiBr_2(PPh_2Me)_2$]	THF	trace
5	[$NiBr_2$(bipy)]	THF	0
6	[$NiBr_2$(dppm)]	THF	72
7	[$NiBr_2$(dppe)]	THF	91
8	[$NiBr_2$(dppp)]	THF	79
9	[$NiBr_2$(dppb)]	THF	58
10	[$NiCl_2$(dppe)]	THF	67
11	[NiI_2(dppe)]	THF	71
12	[$NiBr_2$(dppe)]	CH_2Cl_2	0
13	[$NiBr_2$(dppe)]	diethyl ether	trace
14	[$NiBr_2$(dppe)]	DMF	trace
15	[$NiBr_2$(dppe)]	toluene	43
16	[$NiBr_2$(dppe)]	dioxane	38
17	[$NiBr_2$(dppe)]	ethyl acetate	70
18	[$NiBr_2$(dppe)]	CH_3CN	42
19	[$Pd(dba)_2$]	THF	0
20	[$PdCl_2$(dppe)]	THF	0

[a] Unless stated otherwise, all reactions were carried out by using a Ni catalyst (0.0500 mmol), Zn (2.75 mmol), **1b** (1.50 mmol), and **2a** (1.00 mmol) in a solvent (2.0 mL) at reflux temperature for 24 h under N_2; [b] Yields were determined by ^{1}H NMR analysis with mesitylene as the internal standard.

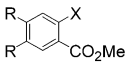
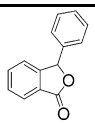
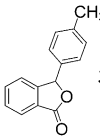
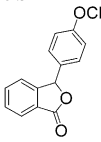
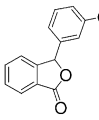
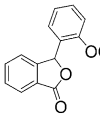
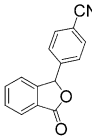
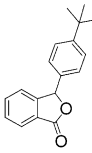
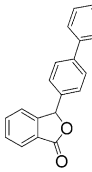
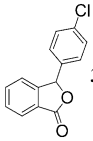
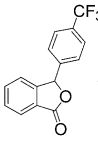
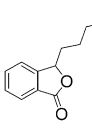
Similar to the reaction with benzaldehyde, the cyclization of **1a** with tolualdehyde (**2b**) and anisaldehyde (**2c**), gave lactonization products **3b** and **3c** in low yields (48 and ~0%, respectively). The product yield improves greatly by using bromobenzoate as the substrate. Thus, **1b** reacts with **2b** and **2c** affording **3b** and **3c** in 91 and 92% yields, respectively (Table 2 entries 4, 6). The lactonization of **1b** was successfully extended to other aldehydes. Treating **1b** with *m*- and *o*-anisaldehyde (**2d**, **2e**) afforded the corresponding lactones **3d** and **3e** in 81 and 86% yields, respectively. The reaction of 4-(*tert*-butyl)benzaldehyde and 4-phenylbenzaldehyde with **1b** produced **3g** and **3h** in excellent yields (Table 2 entries 10, 11). Similarly, the reaction of **1b** with 4-cyanobenzaldehyde (**2f**), 4-chlorobenzaldehyde (**2i**), and 4-(trifluoromethyl)benzaldehye (**2j**) afforded lactones **3f**, **3i**, and **3j** in 80, 61, and 88% yields, respectively, with excellent chemoselectivity (Table 2 entries 9, 12, 13). Under similar conditions, dialdehyde **2m** reacted smoothly with **1b** to give diphthalide derivative **3n** in a 52% yield (Scheme 3). Interestingly, a single isomer was apparent by ^{1}H and ^{13}C NMR,



Scheme 3. Synthesis of a diphthalide derivative.

and single-crystal X-ray analysis of a recrystallized sample illustrated the *meso* stereochemistry. The cyclization reaction can also be applied to aliphatic aldehydes, although in lower yields (entries 14, 15). The present cyclization method was extended to methoxy-substituted bromoester (**1c**), which, when treated with **2b** under standard conditions, produced phthalide **3m** in a 71% yield (entry 16). Overall, the cyclization reaction tolerates a variety of functional groups, such as alkyl, cyano, methoxy, and chloro, on the aromatic ring of aldehydes. The product yield is much less sensitive to the substituent on the aldehyde for 2-bromobenzoate than for 2-iodobenzoate.

Table 2. Results of the nickel-catalyzed cyclization of *o*-haloesters with aldehydes.[a]

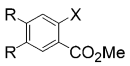
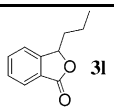
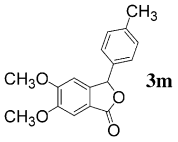
Entry				R^1–CHO	Product	Yield[b] [%]
	R	X		R^1		
1	H	I	**1a**	C_6H_5 (**2a**)	 **3a**	50
2	H	Br	**1b**	(**2a**)	**3a**	86
3	H	I	**1a**	4-MeC_6H_4 (**2b**)	 **3b**	48
4	H	Br	**1b**	(**2b**)	**3b**	91
5	H	I	**1a**	4-$MeOC_6H_4$ (**2c**)	 **3c**	0
6	H	Br	**1b**	(**2c**)	**3c**	92
7	H	Br	**1b**	3-$MeOC_6H_4$ (**2d**)	 **3d**	81
8	H	Br	**1b**	2-$MeOC_6H_4$ (**2e**)	 **3e**	86
9	H	Br	**1b**	4-CNC_6H_4 (**2f**)	 **3f**	80
10	H	Br	**1b**	4-$(CH_3)_3CC_6H_4$ (**2g**)	 **3g**	90
11	H	Br	**1b**	4-$C_6H_5C_6H_4$ (**2h**)	 **3h**	95
12	H	Br	**1b**	ClC_6H_4 (**2i**)	 **3i**	61
13	H	Br	**1b**	4-$CF_3C_6H_4$ (**2j**)	 **3j**	88
14	H	Br	**1b**	$CH_3(CH_2)_5$ (**2k**)	 **3k**	36

Unexpectedly, the reaction of methyl 2-(2-bromophenyl)acetate (**1d**) with **2a** produced six-membered lactone **3o** consisting of *Z* and *E* isomers in a ratio of about 1:3.3 (Scheme 4). The product is evidently from two molecules of aldehyde **2a** and one molecule of **1d**. Condensation of the α-methylene group of **1d** or the subsequent intermediate with **2a** during the reaction explains the formation of **3o**.

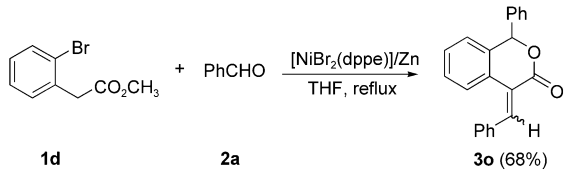
On the basis of the above observations and the known organometallic chemistry of nickel, a catalytic cycle is proposed as shown in Scheme 5. Reduction of nickel(II) to nickel(0) by using zinc powder[15] is likely to initiate the catalytic reaction. Oxidative addition of aryl iodide to the nickel(0) species yields the nickel(II) intermediate **4**. Coordination of an aldehyde molecule to the nickel center, followed by insertion into the nickel–carbon bond, affords nickel–alkoxide intermediate **6**. Attack of the coordinated alkoxy group at the ester moiety of **6** gives the final phthalide derivative **3** and nickel(II). The latter is reduced by zinc powder to regenerate the active nickel(0) species.

A possible reason for the enhanced catalytic activity of bidentate phosphine ligands compared with those that are monodentate is the formation of catalytic intermediates **4** and **5** with *cis* structures. The *cis* arrangement facilitates insertion of the coordinated aldehyde into the nickel–carbon bond in **5** to give intermediate **6**. For a nickel catalyst with monodentate ligands, such as triphenylphosphine, the oxidative addition of aryl halide to nickel(0) generally gives *trans*-[NiL(Ar)X] because of steric repulsion of the two bulky phosphine ligands. The substituents of the *trans* structure are inappropriately positioned for aryl migration to the carbonyl

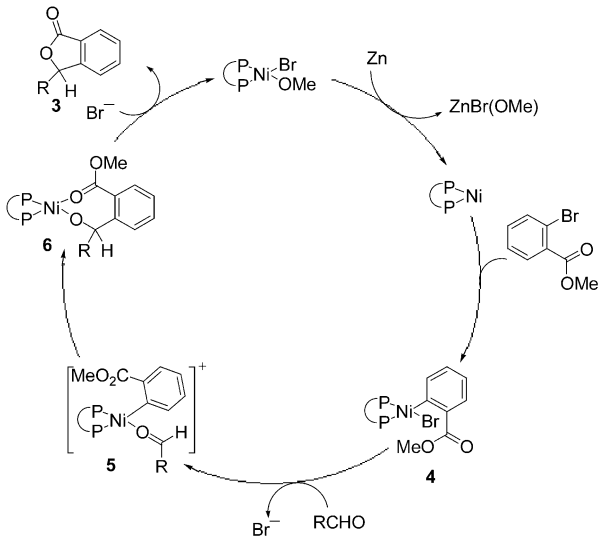
Table 2. (Continued)

Entry				R^1–CHO	Product	Yield[b] [%]
	R	X		R^1		
15	H	Br	**1b**	$CH_3(CH_2)_2$ (**2l**)	 **3l**	24
16	OCH_3	Br	**1c**	(**2b**)	 **3m**	71

[a] Reactions were carried out using the aldehyde (1.0 mmol), organic halide (1.50 mmol), [$NiBr_2$(dppe)] (0.050 mmol, 5.0 mol%), and Zn (2.75 mmol) in THF (2.0 mL) at reflux temperature for 24 h under N_2; [b] Isolated yields were based on the aldehyde used.



Scheme 4. Synthesis of a six-membered lactone.



Scheme 5. Possible mechanism for the nickel-catalyzed cyclization reaction.

carbon of the coordinated aldehyde, thus, greatly reducing the yield of the product.

Unlike the present nickel-catalyzed cyclization reaction, the reaction using palladium complexes as catalysts fails to give the desired lactone product, but instead affords only the homocoupling product (o-$(C_6H_4)CO_2Me)_2$. The difference in catalytic behavior can be attributed to the fact that nickel complexes are generally more labile than palladium species; thus, the substitution of a halide ligand by an aldehyde and the subsequent insertion into the corresponding palladium intermediate is much slower than with nickel, and so does not afford a lactonization product.

Conclusion

In conclusion, we have demonstrated that nickel complexes effectively catalyze the cyclization of o-bromobenzoate with aldehydes to afford phthalide derivatives in excellent yields and with high chemoselectivity under mild conditions. This new reaction provides a remarkable methodology for the construction of phthalide cores in a one-pot reaction. We are now working to explore the full scope of this new catalytic reaction, including an asymmetric version.

Experimental Section

All reactions were conducted under a nitrogen atmosphere on a dual-manifold Schlenk line by using purified deoxygenated solvents and standard inert-atmosphere techniques, unless stated otherwise. Reagents and chemicals were used as purchased, without further purification. [$NiBr_2$(dppe)] was synthesized according to a reported procedure.[16]

General procedure for the cyclization of 2-bromobenzoates (1) with aldehydes (2): A round-bottomed side-arm flask (25 mL) fitted with a reflux condenser containing [$NiBr_2$(dppe)] (0.050 mmol, 5.0 mol%) and zinc powder (2.75 mmol) was evacuated and purged with nitrogen gas three times. Freshly distilled THF (2.0 mL), o-bromobenzoate (1.50 mmol), and aldehyde (1.00 mmol) were sequentially added to the system, and the reaction mixture was stirred under reflux conditions for 24 h. The reaction mixture was cooled to RT, diluted with dichloromethane, and then stirred in air for 15 min. The mixture was filtered through a short Celite and silica-gel pad, and washed with dichloromethane several times. The filtrate was concentrated, and the residue purified on a silica-gel column by using hexanes/ethyl acetate as the eluent, to afford cyclization product **3**.

Spectral data for all new compounds

3-Phenyl-3*H*-isobenzofuran-1-one (3a): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (d, J = 7.6 Hz, 1H), 7.65 (t, J = 7.6 Hz, 1H), 7.55 (t, J = 6.4 Hz, 1H), 7.39–7.32 (m, 6H), 6.40 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.48 (s, C=O), 149.65 (s), 136.40 (s), 134.29 (d), 129.33 (d), 129.27 (d), 128.95 (d), 128.44 (s), 126.94 (d), 125.84 (d), 122.83 (d), 82.68 ppm (d); HRMS: m/z calcd for $C_{14}H_{10}O_2$: 210.0681; found: 210.0683.

3-(4-Methylphenyl)-3*H*-isobenzofuran-1-one (3b): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (d, J = 6.4 Hz, 1H), 7.63 (t, J = 7.6 Hz, 1H), 7.57 (t, J = 7.2 Hz, 1H), 7.31 (d, J = 6.8 Hz, 1H), 7.20–7.14 (m, 4H), 6.38 (s, 1H), 2.35 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.54 (s, C=O), 149.77 (s), 139.28 (s), 134.23 (d), 133.36 (s), 129.59 (d), 129.24 (d), 127.01 (d), 125.66 (s), 125.52 (d), 122.82 (d), 82.73 (d), 21.18 ppm (q); HRMS: m/z calcd for $C_{15}H_{12}O_2$: 224.0837; found: 224.0831.

3-(4-Methoxyphenyl)-3*H*-isobenzofuran-1-one (3c): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93 (d, J = 7.6 Hz, 1H), 7.63 (t, J = 7.2 Hz, 1H), 7.53 (t, J = 7.2 Hz, 1H), 7.29 (d, J = 7.6 Hz, 1H), 7.15 (t, J = 8.8 Hz, 2H), 6.87 (d, J = 8.8 Hz, 2H), 6.35 (s, 1H), 3.78 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.48 (s, C=O), 160.37 (s), 149.71 (s), 134.18 (d), 129.24 (d), 128.73(d), 128.24 (s), 125.88 (s), 125.51 (d), 122.88 (d), 114.27 (d), 82.67 (d), 55.27 ppm (q); HRMS: m/z calcd for $C_{15}H_{12}O_2$: 240.0786; found: 240.0790.

3-(3-Methoxyphenyl)-3*H*-isobenzofuran-1-one (3d): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.91$ (d, $J = 7.6$ Hz, 1H), 7.62 (t, $J = 7.6$ Hz, 1H), 7.51 (t, $J = 7.2$ Hz, 1H), 7.32 (d, $J = 7.6$ Hz, 1H), 7.26 (t, $J = 7.2$ Hz, 1H), 6.88–6.84 (m, 2H), 6.76 (s, 1H), 6.34 (s, 1H), 3.73 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.42$ (s, C=O), 159.91 (s), 149.51 (s), 137.85 (s), 134.26 (d), 129.98(d), 129.28 (d), 125.51 (d), 125.34 (s), 122.76 (d), 118.99 (d), 114.52 (d), 112.32 (d), 82.42 (d), 55.21 ppm (q); HRMS: *m*/*z* calcd for $C_{15}H_{12}O_2$: 240.0786; found: 240.0783.

3-(2-Methoxyphenyl)-3*H*-isobenzofuran-1-one (3e): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.93$ (d, $J = 7.2$ Hz, 1H), 7.60 (t, $J = 6.4$ Hz, 1H), 7.52 (t, $J = 7.2$ Hz, 1H), 7.44 (d, $J = 7.6$ Hz, 1H), 7.31 (t, $J = 7.2$ Hz, 1H), 7.08 (d, $J = 7.6$ Hz, 1H), 6.96 (d, $J = 8.4$ Hz, 1H), 6.90 (t, $J = 7.6$ Hz, 1H), 6.85 (s, 1H), 3.90 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.93$ (s, C=O), 156.95 (s), 150.34 (s), 134.06 (d), 130.08 (d), 128.93 (d), 126.82 (d), 125.57 (s), 125.33 (d), 124.94 (s), 122.87 (d), 120.78 (d), 110.94 (d), 78.01 (d), 55.53 ppm (q); HRMS: *m*/*z* calcd for $C_{15}H_{12}O_2$: 240.0786; found: 240.0781.

4-(3-Oxo-1,3-dihydro-1-isobenzofuranyl)benzonitrile (3f): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.94$ (d, $J = 7.6$ Hz, 1H), 7.67–7.63 (m, 3H), 7.56 (t, $J = 7.2$ Hz, 1H), 7.41 (d, $J = 8.0$ Hz, 2H), 7.31 (d, $J = 7.6$ Hz, 1H), 6.41 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.00$ (s, C=O), 148.47 (s), 141.62 (s), 134.67 (d), 132.79 (d), 129.86 (d), 127.31 (d), 125.98 (d), 125.08 (s), 122.58 (d), 118.07 (s), 113.13 (s), 81.18 ppm (d); HRMS: *m*/*z* calcd for $C_{15}H_9O_2N$: 235.0633; found: 235.0633.

3-[4-(*tert*-Butyl)phenyl]-3*H*-isobenzofuran-1-one (3g): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.94$ (d, $J = 8.0$ Hz, 1H), 7.62 (t, $J = 7.6$ Hz, 1H), 7.54 (t, $J = 6.8$ Hz, 1H), 7.54 (t, $J = 7.2$ Hz, 1H), 7.38 (d, $J = 7.6$ Hz, 2H), 7.35 (d, $J = 7.6$ Hz, 1H), 7.18 (d, $J = 8.4$ Hz, 2H), 6.38 (s, 1H), 1.27 ppm (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.51$ (s, C=O), 152.41 (s), 149.67 (s), 134.17 (d), 133.25 (s), 129.20 (d), 126.78 (d), 125.85 (d), 125.69 (s), 125.51 (d), 122.91 (d), 82.63 (d), 34.61 (s), 31.16 ppm (q); HRMS: *m*/*z* calcd for $C_{18}H_{18}O_2$: 266.1307; found: 266.1312.

3-Biphenyl-4-yl-3*H*-isobenzofuran-1-one (3h): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.97$ (d, $J = 7.2$ Hz, 1H), 7.65 (t, $J = 7.2$ Hz, 1H), 7.59–7.54 (m, 5H), 7.42 (t, $J = 7.6$ Hz, 2H), 7.38–7.32 (m, 4H), 6.44 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.70$ (s, C=O), 149.85 (s), 142.56 (s), 140.51 (s), 135.56 (s), 134.59(d), 129.64 (d), 129.09 (d), 127.93 (d), 127.70 (d), 127.36 (d), 125.93 (d), 123.13 (d), 114.46 (d), 82.72 ppm (d); HRMS: *m*/*z* calcd for $C_{20}H_{14}O_2$: 286.0994; found: 286.0992.

3-(4-Chlorophenyl)-3*H*-isobenzofuran-1-one (3i): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.97$ (d, $J = 7.6$ Hz, 1H), 7.66 (t, $J = 7.2$ Hz, 1H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.35 (d, $J = 7.6$ Hz, 2H), 7.31 (d, $J = 7.6$ Hz, 2H), 7.21 (d, $J = 7.6$ Hz 1H), 6.37 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.44$ (s, C=O), 149.44 (s), 135.55 (s), 135.21 (s), 134.69 (d), 129.81 (d), 129.46 (s), 128.58 (s), 126.02 (d), 125.76 (s), 112.98 (d), 82.08 ppm (d); HRMS: *m*/*z* calcd for $C_{14}H_9ClO_2$: 244.0291; found: 244.0286.

3-(4-Trifluoromethylphenyl)-3*H*-isobenzofuran-1-one (3j): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.97$ (d, $J = 7.2$ Hz, 1H), 7.68–7.63 (m, 2H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.41 (d, $J = 8.0$ Hz, 2H), 7.32 (d, $J = 7.6$ Hz, 2H), 6.43 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.06$ (s, C=O), 148.89 (s), 140.47 (s), 134.53 (d), 131.01 (s), 129.65(d), 127.04 (d), 125.91 (d), 125.75 (d), 125.04 (s), 122.65 (d), 81.44 ppm (d); HRMS: *m*/*z* calcd for $C_{15}H_9F_3O_2$: 278.0555; found: 278.0564.

3-Hexyl-3*H*-isobenzofuran-1-one (3k): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.88$ (d, $J = 7.6$ Hz, 1H), 7.65 (t, $J = 7.6$ Hz, 1H), 7.50 (t, $J = 7.6$ Hz, 1H), 7.41 (d, $J = 7.6$ Hz, 1H), 5.45 (dd, $J = 8.0$, $J = 4.0$ Hz, 1H), 2.04–1.95 (m, 1H), 1.69–1.72 (m, 1H), 1.49–1.40 (m, 2H), 1.38–1.30 (m, 4H), 1.29–1.23 (m, 2H), 0.85 ppm (t, $J = 5.2$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.68$ (s, C=O), 150.13 (s), 133.89 (d), 128.99 (d), 126.15 (s), 125.69 (d), 121.68 (d), 81.44 (d), 34.74 (t), 31.56 (t), 28.97 (t), 24.75 (t), 22.49 (t), 14.00 ppm (q); HRMS: *m*/*z* calcd for $C_{14}H_{18}O_2$: 218.1307; found: 218.1302.

3-Propyl-3*H*-isobenzofuran-1-one (3l): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.87$ (d, $J = 7.6$ Hz, 1H), 7.65 (t, $J = 7.6$ Hz, 1H), 7.50 (t, $J = 7.2$ Hz, 1H), 7.41 (d, $J = 7.2$ Hz, 1H), 5.46 (dd, $J = 8.0$, 4.0 Hz, 1H), 2.01–1.95 (m, 1H), 1.77–1.68 (m, 1H), 1.56–1.35 (m, 2H), 0.92 ppm (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.86$ (s, C=O), 150.36 (s), 133.11 (d), 129.21 (d), 126.39 (s), 125.91 (d), 121.91 (d), 81.47 (d), 34.07 (t), 18.44 (t), 13.99 ppm (q); HRMS: *m*/*z* calcd for $C_{11}H_{12}O_2$: 176.0837; found: 176.0845.

5,6-Dimethoxy-3-(4-methylphenyl)-3*H*-isobenzofuran-1-one (3m): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.30$ (s, 1H), 7.15 (d, $J = 8.0$ Hz, 1H), 7.10 (d, $J = 8.0$ Hz, 1H), 6.64 (s, 1H), 6.22 (s, 1H), 3.92 (s, 3H), 3.84 (s, 3H), 2.31 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 21.4$ (q), 56.5 (q), 82.5 (d), 104.2 (d), 106.0 (d), 117.9 (s), 127.4 (d), 129.8 (d), 133.8 (s), 139.5 (s), 144.5 (s), 150.8 (s), 155.2 (s), 171.0 ppm (s, C=O); HRMS: *m*/*z* calcd for $C_{17}H_{16}O_4$: 284.1049; found: 284.1045.

1,2-Diphthalidylbenzene (3n): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.69$ (d, $J = 7.2$ Hz, 2H), 7.69 (t, $J = 7.6$ Hz, 2H), 7.56 (t, $J = 8.0$ Hz, 2H), 7.46 (d, $J = 7.6$ Hz, 2H), 7.37 (dd, $J = 6.0$, 2.0 Hz, 2H), 7.19 (dd, $J = 6.0$, 2.0 Hz, 2H), 6.39 ppm (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.00$ (s, C=O), 149.21 (s), 134.87 (d), 134.66 (s), 129.89 (d), 129.68 (d), 129.76 (d), 125.46 (s), 123.05 (d), 80.08 ppm (d); HRMS: *m*/*z* calcd for $C_{22}H_{14}O_4$: 342.0892; found: 342.0882.

1-Phenyl-4-[(*E*)-1-phenylmethylidene]-3,4-dihydro-1*H*-3-isochromenone (3o): ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.76$ (s, 1H), 7.45–7.32 (m, 9H), 7.30–7.27 (m, 2H), 7.24 (t, $J = 7.0$ Hz, 1H), 7.14 (td, $J = 7.5$, 1.0 Hz, 1H), 7.03 (d, $J = 8.0$ Hz, 1H), 6.41 ppm (s, 1H); HRMS: *m*/*z* calcd for $C_{22}H_{16}O_2$: 312.1150; found: 312.1154.

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