Note

PIFA-mediated dearomatizative spirocyclization of phenolic biarylic ketones via oxidation and C-C bond cleavage

Guihua Zhao, Biqing Li, Shuangshuang Wang, Man Liu, Yuan Chen, and Bin Wang

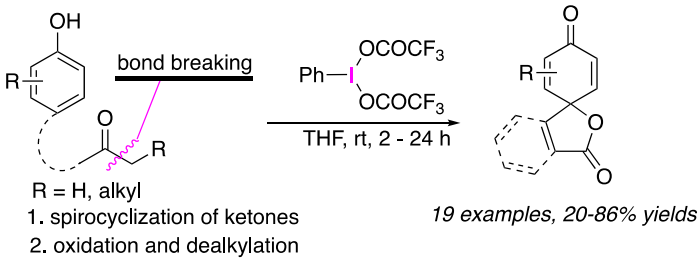
J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.0c00971 • Publication Date (Web): 24 Jun 2020

PIFA-mediated dearomatizative spirocyclization of phenolic biarylic ketones via oxidation and C-C bond cleavage

Gui-Hua Zhao, Bi-Qing Li, Shuang-Shuang Wang, Man Liu, Yuan Chen and Bin Wang*

College of Pharmacy and Tianjin Key Laboratory of Molecular Drug Research, Nankai University, Haihe Education Park, 38 Tongyan Road, Tianjin 300353, P. R. China.

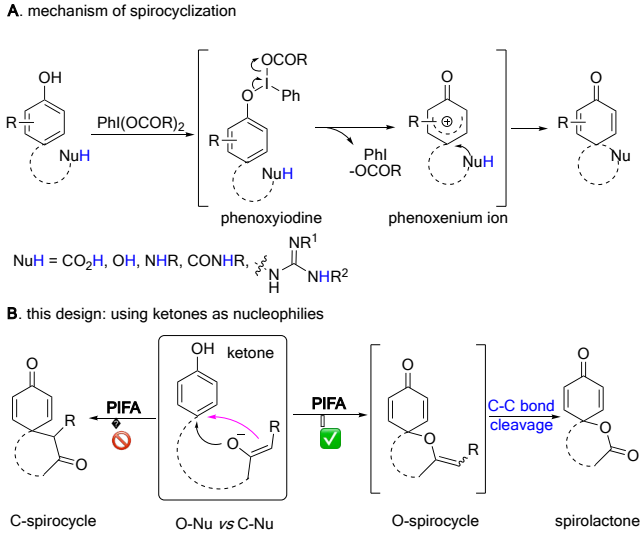
Supporting Information Placeholder



ABSTRACT: The dearomatizing spirocyclization of phenolic biarylic ketones using $PhI(OCOCF_3)_2$ as oxidant is presented. The reaction affords various cyclohexadienones through C-C bond cleavage under mild conditions. Mechanistic investigations reveal that an exocyclic enol ether acts as the key intermediate in the transformation.

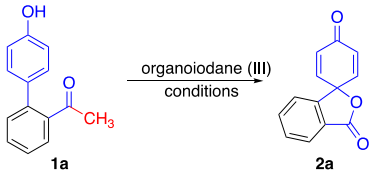
Many elegant synthetic methodologies and strategies have been achieved by the use of hypervalent iodine（III）reagents during the last decades. These environmentally friendly reagents are versatile and play important roles in organic synthesis.[1] One of the most well-known applications of the hypervalent iodine is the use in the dearomatization of phenols to form cyclohexadienones,[2] which were considered valuable intermediates in natural product synthesis.[3] The currently accepted mechanism was that the *para*-substituted phenol initially forms a phenoxyiodine (III) intermediate, which is then converted to a phenoxenium ion through the departure of high-valent iodine atom. The phenoxenium ion is further trapped by an internal nucleophile to offer the final spirodienone (Scheme 1A).[4] This also applies to the dearomatizative cyclization of *ortho*-substituted phenols. The oxygen and nitrogen nucleophiles such as carboxylic acid, alcohol, amine, amide and guanidine, are suitable groups for the spirocyclization.[5] To date, the use of ketones as substrates has been unexplored for this dearomatizing spirocyclization. There are two possible sites of spirocyclization, oxygen or α-carbon of ketone. We envisioned the use of phenolic biarylic ketones as substrates, with the anticipation that such substrates might enable the formation of a five-membered C-spirocycle or (and) an O-spirocycle with an exocyclic double bond, under basic conditions (Scheme 1B). Interestingly, our subsequent studies indicated that the cyclopentanone (C-spirocycle) could not be constructed by this hypervalent iodine-mediated method. We found that an exocyclic enol ether (O-spirocycle) was formed during the reaction. It further underwent oxidation and C-C bond cleavage to afford spirolactone (Scheme 1B). Herein, we report this novel dearomatizative spirocyclization reaction of phenolic biarylic ketones. To our knowledge, this spirocyclization

Scheme 1. Hypervalent iodine-mediated dearomatizative spirocyclization



through the oxidation of ketones and C-C bond breaking is unknown in the hypervalent iodine chemistry.

Table 1. Screening of the reaction conditions[a]



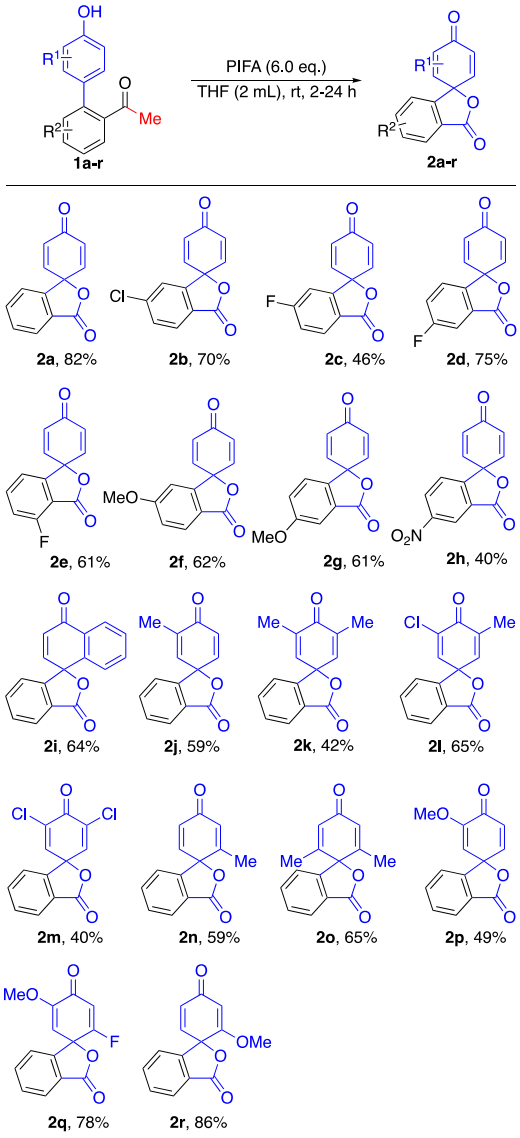
entry	iodine	solvent	base	yield %
1	PIFA (2.5)	THF	EtONa	15
2	PIFA (2.5)	THF	NaOH	0
3	PIFA (2.5)	THF	-	35
4	PIFA (2.5)	DCM	-	25
5	PIFA (2.5)	DME	-	0
6	PIFA (2.5)	CH_3CN	-	0
7	PIFA (4.0)	THF	-	59
8	PIFA (5.0)	THF	-	72
9	PIFA (6.0)	THF	-	82
10	PIFA (7.0)	THF	-	50
11	PIDA (6.0)	THF	-	0
12	PhIO (6.0)	THF	-	0
13	FPIFA (6.0)	THF	-	0
14[b]	PhI (1.0)	THF	-	0

[a]Reaction conditions: **1a** (0.3 mmol), solvent (2 mL), rt, under air, 20 h, isolated yield. PIFA, phenyliodine (III) bis(trifluoroacetate); PIDA, phenyliodine (III) diacetate; FPIFA, pentafluorophenyliodine (III) bis(trifluoroacetate). [b]Oxone or mCPBA (2.5 eq).

We began by testing the combination of phenyliodine (III) bis(trifluoroacetate) (PIFA) and base to effect the spirocyclization of 4-(2-acetylphenyl) phenol **1a** in THF (Table 1). The spirolactone **2a** was obtained in 15% yield with EtONa, while no conversion was observed by use of NaOH (entries 1 and 2). When the reaction was carried out in the absence of base, product **2a** was isolated in higher yield (entry 3). Among various solvents examined, the reaction conducted in THF provided the best results (entries 3-6). Increasing the amount of PIFA from 2.5 equivalents to 4.0-6.0 equivalents dramatically improved the yield of **2a** (entries 7-9). The high-yielding spirocyclization could be achieved by use of 6.0 equiv of PIFA, while further increasing the amount of PIFA to 7.0 equiv led to decreased yield of **2a** due to side reactions (entry 10). Other hypervalent iodine reagents such as phenyl iodine (III) diacetate (PIDA), PhIO, and pentafluorophenyliodine (III) bis(trifluoroacetate) (FPIFA), were also investigated for this dearomatizative spirocyclization (entries 11-13). However, they were completely ineffective because some unknown complex products were formed. As PIFA was used in excess in the present reaction, we attempted to realize a catalytic transformation by use of the combination of PhI/Oxone or PhI/mCPBA, but they proved to be unsuccessful (entry 14).

Having developed the effective conditions for the spiroannulation, the scope of the substrates was further investigated. First, the reactivity of phenyl methyl ketone moiety with different substitutes on the phenyl ring was tested (Table 2, **1b-h**). These substrates with chloro, fluoro, methoxyl and nitro groups underwent the spirocyclization smoothly, furnishing the desired products **2b-h** in moderate to good yields. The structure of **2b** was confirmed unambiguously by single crystal X-ray diffraction.[6] Among the fluoro-substituted substrates **1c-e**, the *para*-fluoro-biphenylic ketone **1d** was found to give the highest yield. In the cases of methoxyl-substituted **1f** and **1g**, the position of methoxyl group on the phenyl ring had no influence on the yield. Variations in the substituents of phenol moiety were further evaluated (Table 2, **1i-r**). Substrate **1i** with a naphthol moiety was compatible with the reaction, producing **2i** in 64% yield. Furthermore, phenols

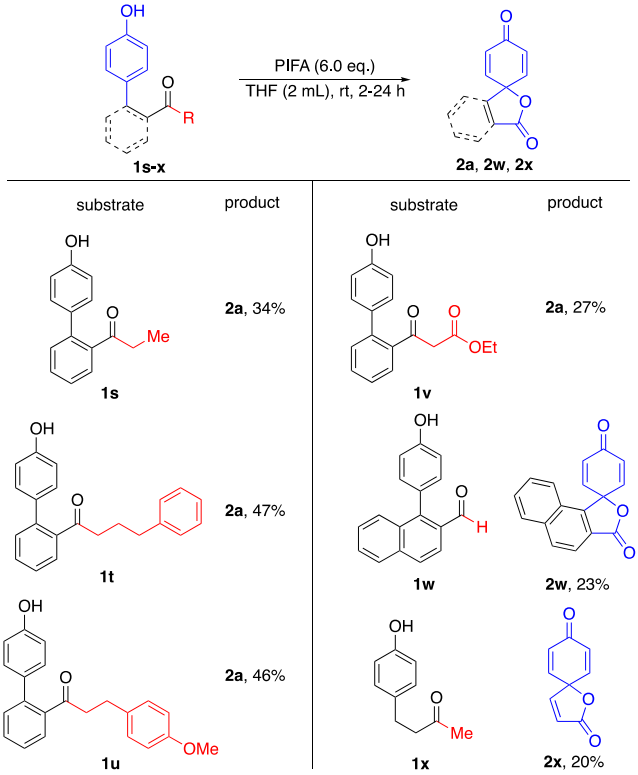
Table 2. Scope of the phenolic biarylic ketones[a]



[a]Reaction conditions: **1a-r** (0.3 mmol), PIFA (1.8 mmol), THF (2 mL), rt, under air, 2-24 h , determined by TLC, isolated yield.

with dimethyl, methyl/chloro, dichloro, methoxyl/fluoro groups on their *ortho*- or *meta*-positions reacted smoothly, affording products **2k-m**, **2o** and **2q** in 40-78% yields. Surprisingly, *meta*-methoxyl substituted substrate **1r** gave the desired product **2r** in 86% yield, which was much higher than that of *ortho*-methoxyl substituted substrate **1p** (49%). It indicated that the efficiency of annulation was not influenced by the steric hindrance of methoxyl group. Instead, the presence of a methoxyl group adjacent to the reaction site improved the spirocyclization. A similar promotion from *meta*-methyl groups was also observed in the reaction of **1o** (65%), which gave higher yield than **1k** (42%).

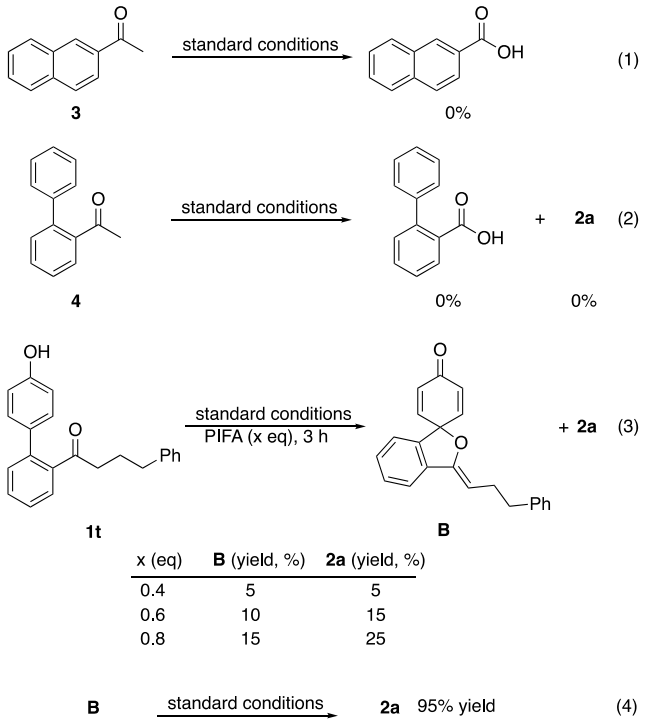
Table 3. Scope of the phenolic biarylic ketones with long alkyl side chain[a]



[a]Reaction conditions: **1s-x** (0.3 mmol), PIFA (1.8 mmol), THF (2 mL), rt, under air, 7-24 h, determined by TLC, isolated yield.

We then investigated other potential substrates in this transformation (Table 3). When the ketones with long alkyl chains, including ethyl, phenylpropyl and (4-methoxyphenyl) ethyl groups, were subjected to the spirocyclization conditions, the spirocyclization occurred to afford product **2a** in moderate yields (Table 3, **1s-u**). Surprisingly, the phenolic biaryl substrates containing β-ketoester and aldehyde functional groups could also undergo the dearomatizing spirocyclization to give the corresponding products **2a** and **2w**, albeit in low yields. In addition, the reaction constructed a γ-crotolactone on the *para*-position of phenol by use of 4-(4-hydroxyphenyl)-2-butanone **1x**. A dehydrogenation of five-membered spirocycle was achieved by this strategy (**2x**). This kind of product could not be obtained by the existing hypervalent-iodine (III)-mediated spirocyclization of carboxylic acid.[5b]

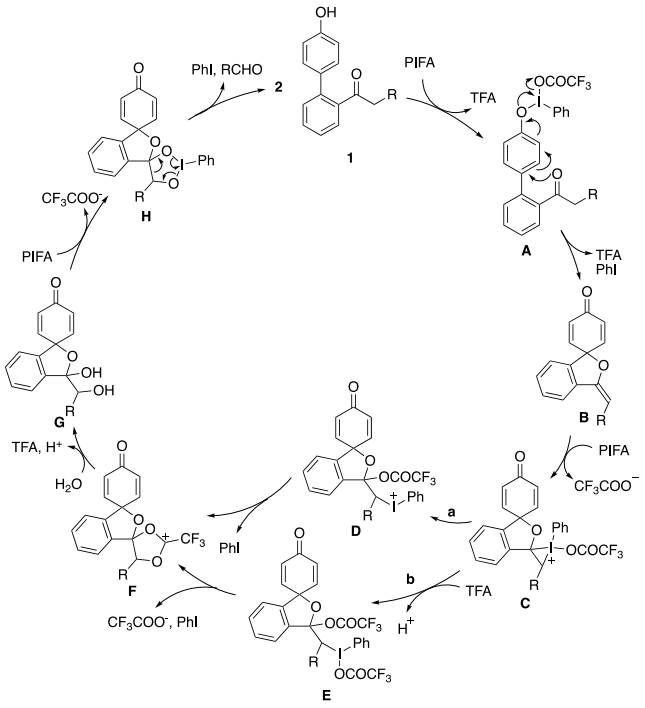
Scheme 2. Control experiments



After the investigation of substrate scope, we performed control experiments to explore the reaction mechanism (Scheme 2). When 2-acetylnaphthalene **3** and 2'-phenylacetophenone **4** were respectively subjected to the standard reaction conditions, the acetyl group remained intact and no reaction was observed (eqs 1 and 2). The results excluded the possibility that the corresponding carboxylic acids were the intermediates of the spirocyclization. We then carried out the experiments of **1t** by reducing the amount of PIFA from 0.8 to 0.4 equiv (eq 3). The reaction produced the desired product **2a** and simultaneously afforded an exocyclic enol ether **B** after 3 hours. The transformation of **B** leading to **2a** was further achieved by the addition of PIFA and prolonging reaction time. Compound **B** was isolated and its structure was confirmed by NMR and HR MS. It was further subjected to the present spirocyclization conditions. Product **2a** was formed in almost quantitative yield (eq 4). These results suggest that enol ether **B** is most likely an intermediate of the present spirocyclization. Unfortunately, attempts to capture the fragment from phenylpropyl group of **1t** failed. We propose that this alkyl moiety is further oxidized by PIFA to the undetectable small molecules.[7]

Based on our results and previous reports,[7-8] a mechanism for the spirocyclization was proposed (Scheme 3). First, the phenolic oxygen of substrate **1** attacks PIFA to give intermediate **A**, which further underwent intramolecular spirocyclization to afford enol ether **B**. The excess PIFA then reacted with alkene moiety of **B** to form intermediate **C**,[1e, 8a] which was converted to cyclic intermediate **F**[8a,9] through two possible pathways. In pathway **a**, an intramolecular rearrangement of **C** occurred to yield intermediate **D**. Intermediate **C** could also react with TFA through addition/elimination, resulting in the formation of intermediate **E** (pathway **b**).[8a] The hydrolysis of **F** gave glycol intermediate **G**, which afforded the final product **2a** and aldehyde through the well-established hypervalent iodine (III)-mediated oxidation and C-C bond cleavage of glycols.[7, 10]

Scheme 3. proposed mechanism



In conclusion, we have developed a spirocyclization reaction using phenolic biarylic ketones as starting materials under mild conditions. This novel transformation involves dearomatization/oxidation/C-C bond cleavage processes. The proposed mechanism is supported by the isolation and identification of an exocyclic enol ether intermediate.

EXPERIMENTAL SECTION

General Remarks

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AVANCE AV400 (400 MHz for H and 101 MHz for C). Signal positions were recorded in ppm with the abbreviations s, d, t, q, and m denoting singlet, doublet, triplet, quartet, and multiplet respectively. All NMR chemical shifts were referenced to residual solvent peaks or to $Si(CH_3)_4$ as an internal standard. NMR Spectra recorded in $CDCl_3$ were referenced to residual $CHCl_3$ at 7.26 ppm for ^{1}H or 77.0 ppm for ^{13}C. NMR spectra recorded in DMSO-d_6 were referenced to residual DMSO at 2.49 ppm and 3.33 ppm for ^{1}H or 39.6 ppm for ^{13}C. All coupling constants *J* were quoted in Hz. Data were reported as follows: chemical shift, multiplicity, coupling constant and integration. HRMS were measured using Q-TOF LC–MS and the ESI-FTICR technique. Reactions were monitored by thin-layer chromatography (TLC) on 0.25mm silica gel glass plates coated with 60 F254. Column chromatography

was performed on silica gel (200-300 mesh) using a mixture of petroleum ether (60-90°C) and ethyl acetate as eluant. All reagents were weighed and handled in air at room temperature and all reactions were performed under an air atmosphere. Commercially available reagents were used as received without further purification. Reactants **1x** were purchased from commercial sources, and reactants **1a-h**, **1s-u**, **1v**, **1i-1r** were prepared by the known method[11]and analytical data matched literature values.

General Procedure for the Preparation of Products 2a-r, 2w, 2x

Substrate **1** (0.3 mmol, 1 equiv) was added to PIFA (1.8 mmol, 774.07 mg, 6.0 equiv) under air, and THF (2 mL) were added. After the mixture was stirred at room temperature for 2-24 h, the residue was mixed with silica gel and concentrated. The resulting mixture was purified by silica gel column chromatography on silica gel with petroleum ether and EtOAc as eluent to give the desired product **2**.

Large Scale for the Synthesis of Product 2a.

Substrate 1-(4'-hydroxy-[1,1'-biphenyl]-2-yl)ethan-1-one **1a** (1 mmol, 1.0 equiv) was added to PIFA (6.0 mmol, 2580 mg, 6.0 equiv) under air, and THF (7mL) were added. After the mixture was stirred at room temperature for 20 h, the residue was mixed with silica gel and concentrated. The resulting mixture was purified by silica gel column chromatography on silica gel with petroleum ether: EtOAc (10:1) as eluent to give the desired product **2a** (141 mg, 66%).

3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-diene-3',4-dione (**2a**).[12] Following general procedure **1a** in 0.3 mmol scale. Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1:10), colorless solid (52.1 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (t, *J* = 5.2 Hz, 1H), 7.78 – 7.61 (m, 2H), 7.32 (dd, *J* = 7.9, 2.9 Hz, 1H), 6.67 (dd, *J* = 9.8, 3.1 Hz, 2H), 6.43 (dd, *J* = 9.9, 3.1 Hz, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 184.3, 169.0, 146.6, 144.3, 135.23, 130.7, 129.9, 126.8, 125.6, 122.5, 80.4. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{13}H_8O_3Na$ 235.0366; found, 235.0369.

6'-chloro-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-diene-3',4-dione (**2b**).[13] Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1:10), white solid (51.3 mg, 70%). 1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.2 Hz, 1H), 7.61 (dd, J = 8.1, 1.7 Hz, 1H), 7.29 (d, J = 1.7 Hz, 1H), 6.70 – 6.59 (m, 2H), 6.50 – 6.38 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 183.9, 167.8, 148.4, 143.5, 142.1, 131.5, 130.3, 127.9, 124.1, 122.9, 79.8. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{13}H_8ClO_3$ 247.0162; found, 247.0161.

6'-fluoro-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-diene-3',4-dione (**2c**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1:10), colorless solid (35.3 mg, 46%). Mp: 172-178 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.05 (dd, J = 9.1, 4.7 Hz, 1H), 7.55 (ddt, J = 7.0, 4.3, 2.1 Hz, 2H), 7.05 – 6.93 (m, 2H), 6.52 – 6.36 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 184.5, 168.2, 168.1, 165.5, 150.2, 150.1, 130.5, 129.3, 122.4, 119.3, 119.1, 111.0, 110.8, 80.1. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{13}H_8FO_3$ 231.0457; found, 231.0483.

5'-fluoro-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-diene-3',4-dione (**2d**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1:10), yellow oil (51.8mg, 75%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, J = 6.9, 2.4 Hz, 1H), 7.46 (td, J = 8.5, 2.4 Hz, 1H), 7.32 (dd, J = 8.4, 4.2 Hz, 1H), 6.73 – 6.59 (m, 2H), 6.51 – 6.36 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 184.0, 167.7, 165.2 , 162.7, 143.9, 142.1, 130.1, 123.4, 123.2, 113.1, 80.3. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{13}H_8FO_3$ 231.0457; found, 231.0456.

4'-fluoro-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-diene-3',4-dione (**2e**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1:10), colorless oil (42.6 mg, 61%) ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.85 (td, J = 8.0, 4.7 Hz, 1H), 7.50 (t, J = 8.9 Hz, 1H), 7.32 (d, J = 7.7 Hz, 1H), 7.06 (d, J = 9.7 Hz, 2H), 6.44 (d, J = 9.8 Hz, 2H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 184.6, 165.5, 165.5, 160.6, 157.9, 149.3, 138.7, 138.6, 130.1, 119.6, 119.6, 117.9, 117.7, 114.0, 113.9, 80.4. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{13}H_8FO_3$ 231.0457; found, 231.0450.

6'-methoxy-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-diene-3',4-dione (**2f**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1:10), yellow solid (44.8 mg, 62%). Mp: 218-228 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.87 (d, J = 8.5 Hz, 1H), 7.21 (dd, J = 8.6, 2.2 Hz, 1H), 7.04 (d, J = 2.1 Hz, 1H), 6.96 (d, J = 9.7 Hz, 2H), 6.41 (d, J = 9.9 Hz, 2H), 3.85 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 184.7, 168.8, 165.6, 150.1, 145.3, 130.1, 128.1, 118.9, 117.9, 106.9, 80.0, 56.8. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{14}H_{11}O_4$ 243.0657; found, 243.0648.

5'-methoxy-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-diene-3',4-dione (**2g**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1:10), yellow oil (44.3 mg, 61%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.44 (d, J = 2.2 Hz, 1H), 7.41 – 7.33 (m, 2H), 7.00 – 6.93 (m, 2H), 6.42 – 6.36 (m, 2H), 3.88 (s, 3H).^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 184.7, 169.1, 161.8, 145.8, 138.7, 129.7, 127.5, 124.3, 123.9, 109.2, 80.5, 56.6. HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{14}H_{11}O_4Na$ 265.0471; found, 265.0475.

5'-nitro-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-diene-3',4-dione (**2h**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1:10), yellow solid (30.8 mg, 40%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.64 (d, J = 2.1 Hz, 1H), 8.58 (dd, J = 8.4, 2.2 Hz, 1H), 7.84 (d, J = 8.4 Hz, 1H), 7.07 (d, J = 9.9 Hz, 2H), 6.49 (d, J = 9.9 Hz, 2H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 184.4, 167.5, 152.1, 150.0, 144.0, 130.7, 130.4, 128.0, 125.2, 121.5, 81.0.

3H,4'H-spiro[isobenzofuran-1,1'-naphthalene]-3,4'-dione (**2i**).[14] Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1:10), russet solid (48.2 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 – 8.18 (m, 1H), 8.08 – 8.00 (m, 1H), 7.66 – 7.56 (m, 2H), 7.55 – 7.48 (m, 2H), 7.13 – 7.05 (m, 1H), 7.04 – 6.97 (m, 1H), 6.78 (d, J = 10.1 Hz, 1H), 6.61 (d, J = 10.1 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 183.53, 169.7,150.2, 144.7, 139.0, 135.3, 133.6, 130.2, 130.0, 129.5,

127.2, 126.5, 126.5, 125.1, 122.6, 81.6. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{17}H_{11}O_3$ 263.0703; found, 263.0700.

3-methyl-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-diene-3',4-dione (**2j**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1:10), brown solid (39.5 mg, 59%). Mp: 152-158 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (dd, J = 7.5, 2.7 Hz, 1H), 7.66 (dtd, J = 36.9, 7.3, 3.0 Hz, 2H), 7.34 – 7.22 (m, 1H), 6.62 (dt, J = 9.8, 3.1 Hz, 1H), 6.41 (dd, J = 9.7, 2.9 Hz, 2H), 1.97 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 185.1, 144.0, 139.4, 137.1, 130.5, 129.9, 126.7, 122.4, 15.7. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{14}H_{12}O_3$ 227.0708; found, 227.0706.

3,5-dimethyl-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-diene-3',4-dione (**2k**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1:10), gray solid (30.3 mg, 42%). Mp: 148-150 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (dt, J = 7.6, 1.0 Hz, 1H), 7.69 (td, J = 7.5, 1.2 Hz, 1H), 7.60 (td, J = 7.5, 1.0 Hz, 1H), 7.28 – 7.25 (m, 1H), 6.40 (d, J = 1.2 Hz, 2H), 1.98 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 185.9, 169.3, 147.8, 139.1, 136.9, 134.9, 130.2, 126.6, 125.8, 122.4, 81.3, 15.9. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{15}H_{13}O_3$ 241.0865; found, 241.0867, 242.0880.

3-chloro-5-methyl-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-diene-3',4-dione (**2l**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1:10), yellow solid (49.8 mg, 65%). Mp: 129-135°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 – 7.96 (m, 1H), 7.75 (t, J = 7.5 Hz, 1H), 7.65 (t, J = 7.5 Hz, 1H), 7.34 (d, J = 7.7 Hz, 1H), 6.81 (d, J = 3.0 Hz, 1H), 6.46 (dd, J = 3.3, 1.7 Hz, 1H), 2.04 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 178.5, 168.6, 146.2, 139.6, 136.6, 135.3, 134.4, 130.8, 126.9, 125.6, 122.5, 81.33, 16.2. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{14}H_{10}ClO_3$ 261.0318; found:261.0316.

3,5-dichloro-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-diene-3',4-dione (**2m**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1:10), pale yellow solid (39.6 mg, 40%). Mp: 197-199 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (dt, J = 7.5, 0.9 Hz, 1H), 7.75 (dtd, J = 37.8, 7.5, 1.1 Hz, 2H), 7.41 (dt, J = 7.8, 0.9 Hz, 1H), 6.86 (s, 2H).^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 171.9, 167.8, 144.8, 140.3, 135.6, 133.5, 131.4, 127.3, 125.4, 122.6, 81.2. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{13}H_7Cl_2O_3$ 280.9772; found, 280.9765.

2-methyl-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-diene-3',4-dione (**2n**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1:10), white solid (39.6 mg, 59%). Mp: 86-95 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 7.6 Hz, 1H), 7.69 (dt, J = 34.6, 7.5 Hz, 2H), 7.24 (d, J = 7.7 Hz, 1H), 6.63 (dd, J = 9.9, 1.4 Hz, 1H), 6.46 – 6.23 (m, 2H), 1.66 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 185.0, 169.4, 154.2, 147.3, 144.7, 135.3, 129.4, 128.5, 126.6, 125.9, 122.0, 82.6, 17.2. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{14}H_{11}O_3$ 227.0708; found, 227.0709.

2,6-dimethyl-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-diene-3',4-dione (**2o**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1:10), brown oil (47.1 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 7.7 Hz, 1H), 7.69 (dtd, J = 32.5, 7.4, 1.0 Hz, 2H), 7.21 (d, J = 7.6 Hz, 1H), 6.27 (s, 2H), 1.65 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 184.9, 169.9, 154.6, 148.1, 135.4, 130.6, 126.4, 126.1, 121.4, 17.1. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{15}H_{13}O_3$ 241.0865; found, 241.0866.

3-methoxy-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-diene-3',4-dione (**2p**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1:10), pale yellow solid (35.5 mg, 49%). Mp: 176-182 °C.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (dt, J = 7.6, 1.0 Hz, 1H), 7.69 (dtd, J = 38.7, 7.5, 1.1 Hz, 2H), 7.33 (dt, J = 7.7, 0.9 Hz, 1H), 6.65 (dd, J = 9.9, 2.7 Hz, 1H), 6.42 (d, J = 10.0 Hz, 1H), 5.57 (d, J = 2.8 Hz, 1H), 3.69 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 179.8, 169.0, 151.5, 147.8, 144.9, 135.2, 130.5, 129.1, 126.7, 125.6, 122.4, 111.3, 82.6, 55.4. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{14}H_{11}O_4$ 243.0657; found, 243.0658.

2-fluoro-5-methoxy-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-diene-3',4-dione (**2q**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1:10), white solid (61.2 mg, 78%). Mp: 193-196 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (dt, J = 7.6, 1.0 Hz, 1H), 7.77 (td, J = 7.5, 1.2 Hz, 1H), 7.69 (td, J = 7.5, 1.0 Hz, 1H), 7.39 (dt, J = 7.8, 1.0 Hz, 1H), 6.15 (d, J = 10.9 Hz, 1H), 5.42 (d, J = 9.1 Hz, 1H), 3.72 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 180.7, 171.1, 168.2, 151.4, 145.3, 135.4, 131.2, 126.7, 126.1, 122.2, 110.1, 107.2, 80.9, 556.0. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{14}H_{10}FO_4$ 261.0563; found, 261.0559.

2-methoxy-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-diene-3',4-dione (**2r**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1:10), yellow solid (62.7 mg, 86%). Mp: 142-146 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (dt, J = 7.6, 1.1 Hz, 1H), 7.68 (dtd, J = 30.8, 7.5, 1.1 Hz, 2H), 7.28 (dt, J = 7.7, 0.9 Hz, 1H), 6.51 – 6.34 (m, 2H), 5.72 (d, J = 1.5 Hz, 1H), 3.64 (s, 3H).^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 186.2, 169.0, 146.8, 140.1, 135.0, 130.6, 129.7, 126.5, 126.1, 121.7, 103.0, 80.3, 56.4. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{14}H_{11}O_4$ 243.0657; found, 243.0658.

3'H-spiro[cyclohexane-1,1'-naphtho[1,2-c]furan]-2,5-diene-3',4-dione (**2w**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1:10), yellow oil (19.6 mg, 23%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (dd, J = 20.5, 8.3 Hz, 2H), 7.95 (d, J = 8.4 Hz, 1H), 7.81 – 7.68 (m, 2H), 7.67 – 7.57 (m, 1H), 6.81 – 6.69 (m, 2H), 6.67 – 6.54 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 184.4, 144.9, 144.3, 136.7, 132.5, 131.1, 129.6, 128.6, 126.5, 124.2, 122.8, 120.9, 79.5. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{17}H_{10}O_3Na$ 285.0528; found, 285.0528.

1-oxaspiro[4.5]deca-3,6,9-triene-2,8-dione (**2x**).[15] Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1/5), colorless solid (10 mg, 20%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (d, J = 5.5 Hz, 1H), 6.61 – 6.51 (m, 2H), 6.46 – 6.39 (m, 2H), 6.36 (d, J = 5.4 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 183.6, 171.3, 154.4, 131.3, 123.6, 81.9. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_9H_7O_3$ 163.0395; found, 163.0391.

1-(4'-hydroxy-[1,1'-biphenyl]-2-yl)ethan-1-one (**1a**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1/15), white solid (78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.46 (m, 2H), 7.38 (d, J = 7.4 Hz, 2H), 7.19 (dd, J = 8.5, 2.3 Hz, 2H), 6.89 (dd, J = 8.5, 2.3 Hz, 2H), 6.50 (s, 1H), 2.06 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 206.9, 156.2, 140.6, 132.7, 131.0, 130.3, 127.8, 127.1, 30.5. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{14}H_{13}O_2$ 213.0916; found, 213.0912.

1-(5-chloro-4'-hydroxy-[1,1'-biphenyl]-2-yl)ethan-1-one (**1b**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1/15), white solid (75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, J = 8.1 Hz, 1H), 7.40 – 7.33 (m, 2H), 7.20 – 7.08 (m, 3H), 6.93 – 6.87 (m, 2H), 2.06 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 206.0, 156.7, 142.4, 138.6, 137.1, 130.3, 130.1, 129.5, 127.2, 116.0, 30.4. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{14}H_{12}ClO_2$ 247.0526; found, 247.0519.

1-(5-fluoro-4'-hydroxy-[1,1'-biphenyl]-2-yl)ethan-1-one (**1c**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1/15), yellow solid (85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (dd, J = 9.4, 5.7 Hz, 1H), 7.23 – 7.15 (m, 2H), 7.07 (ddt, J = 8.2, 3.8, 2.0 Hz, 2H), 6.94 – 6.85 (m, 2H), 2.05 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 205.1, 165.1, 162.6, 156.6, 143.5, 136.7, 131.7, 130.6, 130.5, 130.0, 117.2, 116.9, 115.9, 114.2, 114.0, 30.4. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{14}H_{12}FO_2$ 231.0816; found, 231.0812.

1-(4-fluoro-4'-hydroxy-[1,1'-biphenyl]-2-yl)ethan-1-one (**1d**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1/15), yellow solid (85%). Mp: 130-136 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.24 (m, 5H), 5.42 (dd, J = 7.6, 5.7 Hz, 1H), 3.23 (dd, J = 15.7, 7.7 Hz, 1H), 2.81 (dd, J = 15.7, 5.6 Hz, 1H), 1.94 (ddd, J = 12.4, 7.9, 4.6 Hz, 1H), 1.21 (s, 9H), 1.06 – 0.94 (m, 2H), 0.89 – 0.79 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 207.8, 140.1, 128.3, 128.0, 127.0, 82.0, 80.6, 48.6, 26.4, 21.3, 11.1, 11.0. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{14}H_{12}FO_2$ 231.0816; found, 231.0811.

1-(3-fluoro-4'-hydroxy-[1,1'-biphenyl]-2-yl)ethan-1-one (**1e**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1/15), white solid (78%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (td, J = 8.0, 5.7 Hz, 1H), 7.16 (dd, J = 7.9, 5.2 Hz, 3H), 7.08 (t, J = 8.9 Hz, 1H), 6.87 – 6.78 (m, 2H), 2.26 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 203.2, 160.0, 157.5, 156.2, 141.3, 131.0, 130.9, 130.1, 125.8, 115.8, 114.2, 32.4. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{14}H_{12}FO_2$ 231.0816; found, 231.0819.

1-(4'-hydroxy-5-methoxy-[1,1'-biphenyl]-2-yl)ethan-1-one (**1f**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1/15), yellow solid (68%). Mp: 134-136 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.63 (s, 1H), 7.53 (d, J = 8.6 Hz, 1H), 7.16 – 7.09 (m, 2H), 6.96 (dd, J = 8.6, 2.6 Hz, 1H), 6.88 – 6.80 (m, 3H), 3.84 (s, 3H), 1.99 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 202.3, 161.4, 157.9, 143.3, 133.2, 131.6, 130.7, 130.3, 115.9, 115.6, 112.8, 55.9, 30.5. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{15}H_{15}O_3$ 243.1016; found, 243.1018.

1-(4'-hydroxy-4-methoxy-[1,1'-biphenyl]-2-yl)ethan-1-one (**1g**).[16] Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1/15), pale yellow oil (78%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.56 (s, 1H), 7.29 (d, J = 8.5 Hz, 1H), 7.13 – 7.03 (m, 3H), 7.01 (d, J = 2.7 Hz, 1H), 6.85 – 6.78 (m, 2H), 3.81 (s, 3H), 2.04 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 204.2, 158.4, 157.4, 141.8, 132.8, 131.8, 131.0, 130.2, 116.9, 116.0, 112.8, 55.9, 30.7. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{15}H_{15}O_3$ 243.1016; found, 243.1019.

1-(4'-hydroxy-4-nitro-[1,1'-biphenyl]-2-yl)ethan-1-one (**1h**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1/15), yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.91 (s, 1H), 8.35 (dd, J = 8.5, 2.5 Hz, 1H), 8.29 (d, J = 2.5 Hz, 1H), 7.69 (d, J = 8.5 Hz, 1H), 7.21 (d, J = 8.2 Hz, 2H), 6.90 (d, J = 8.3 Hz, 2H), 2.15 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 202.7, 159.0, 146.5, 146.4, 141.4, 132.0, 130.6, 129.0, 125.5, 123.1, 30.5.

1-(2-(4-hydroxynaphthalen-1-yl)phenyl)ethan-1-one (**1i**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1/15), yellow solid (60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 – 8.25 (m, 1H), 7.73 (dd, J = 7.7, 1.5 Hz, 1H), 7.68 – 7.60 (m, 1H), 7.60 – 7.40 (m, 5H), 7.10 (d, J = 7.6 Hz, 1H), 6.89 (d, J = 8.4 Hz, 1H), 6.75 (d, J = 7.7 Hz, 1H), 1.83 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 205.6, 152.3, 141.6, 139.3, 132.9, 132.1, 130.9, 130.5, 128.2, 127.9, 127.5, 127.1, 125.5, 125.3, 124.7, 122.4, 108.1, 29.8. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{18}H_{15}O_2$ 263.1067; found, 263.1067.

1-(4'-hydroxy-3'-methyl-[1,1'-biphenyl]-2-yl)ethan-1-one (**1j**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1/15), yellow solid (85%). Mp: 77-80 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.45 (m, 2H), 7.40 – 7.34 (m, 2H), 7.12 (d, J = 2.3 Hz, 1H), 6.99 (dd, J = 8.1, 2.3 Hz, 1H), 6.80 (d, J = 8.1 Hz, 1H), 2.28 (s, 3H), 2.05 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 206.8, 154.4, 140.7, 132.7, 131.3, 130.9, 130.2, 127.8, 127.7, 126.9, 124.7, 115.2, 30.5. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{15}H_{15}O_2$ 227.1067; found, 227.1069.

1-(4'-hydroxy-3',5'-dimethyl-[1,1'-biphenyl]-2-yl)ethan-1-one (**1k**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1/15), brown solid (80%). Mp: 120-122 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.43 (m, 2H), 7.34 (ddd, J = 8.9, 7.2, 1.3 Hz, 2H), 6.94 (s, 2H), 2.27 (s, 6H), 2.03 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 206.3, 152.7, 140.7, 132.5, 130.8, 130.2, 129.1, 127.8, 126.8, 123.9, 30.5, 16.1. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{16}H_{17}O_2$ 241.1223; found, 241.1227.

1-(3'-chloro-4'-hydroxy-5'-methyl-[1,1'-biphenyl]-2-yl)ethan-1-one (**1l**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1/15), brown solid (75%). Mp: 88-91 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (dd, J = 7.6, 1.5 Hz, 1H), 7.49 (td, J = 7.5, 1.5 Hz, 1H), 7.40 (td, J = 7.5, 1.3 Hz, 1H), 7.33 (dd, J = 7.6, 1.3 Hz, 1H), 7.17 (d, J = 2.2 Hz, 1H), 7.01 (dd, J = 2.0, 1.0 Hz, 1H), 5.74 (s, 1H), 2.32 (s, 3H), 2.09 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 204.7, 149.5, 140.6, 139.1, 133.4, 130.8, 130.2, 127.5, 126.4, 126.3, 119.8, 30.5, 16.4. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{15}H_{14}ClO_2$ 261.0677; found, 261.0678.

3-(*tert*-butylperoxy)-3-(naphthalen-2-yl)-1-phenylpropan-1-one (**1m**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1/15), pale yellow solid (52%). Mp: 126-128 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.56 (m, 1H), 7.51 (td, J = 7.5, 1.5 Hz, 1H), 7.44 (td, J = 7.5, 1.3 Hz, 1H), 7.34 – 7.29 (m, 1H), 7.26 (d, J = 5.0 Hz, 2H), 2.20 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 203.5, 140.2, 137.8, 134.4, 131.1, 130.4, 128.5, 128.3, 128.1, 121.3, 30.4. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{14}H_{11}Cl_2O_2$ 281.0131; found, 281.0128.

1-(4'-hydroxy-2'-methyl-[1,1'-biphenyl]-2-yl)ethan-1-one (**1n**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1/15), brown oil (42%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.58 (m, 1H), 7.53 – 7.32 (m, 2H), 7.24 (dd, J = 7.6, 1.5 Hz, 1H), 6.98 – 6.60 (m, 4H), 2.07 (d, J = 6.5 Hz, 3H), 2.02 – 1.95 (m, 3H).^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 205.4, 156.0, 140.5, 137.1, 132.6, 131.2, 131.1, 130.8, 128.1, 127.2, 117.2, 29.9, 20.3. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{15}H_{15}O_2$ 227.1067; found, 227.1069.

1-(4'-hydroxy-2',6'-dimethyl-[1,1'-biphenyl]-2-yl)ethan-1-one (**1o**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1/15), brown solid (60%). Mp: 52-55 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 7.8 Hz, 1H), 7.47 (dt, J = 44.4, 7.5 Hz, 3H), 7.13 (d, J = 7.6 Hz, 1H), 6.60 (s, 2H), 2.00 (s, 3H), 1.92 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 155.2, 140.1, 139.6, 137.4, 132.7, 131.7, 131.2, 128.6, 127.3, 29.3, 20.8. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{16}H_{17}O_2$ (M+H)$^+$: 241.1223; found, 241.1228.

3-(*tert*-butylperoxy)-1-phenyl-3-(thiophen-2-yl)propan-1-one (**1p**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1/15), brown oil (74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.46 (m, 2H), 7.39 (ddd, J = 7.4, 4.3, 2.7 Hz, 2H), 6.98 (d, J = 8.0 Hz, 1H), 6.89 – 6.81 (m, 2H), 3.89 (s, 3H), 2.02 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 205.6, 146.7, 145.7, 141.1, 140.3, 132.8, 130.6, 130.1, 127.7, 127.2, 122.0, 114.8, 111.5, 56.1. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{15}H_{15}O_3$ 243.1016; found, 243.1019.

1-(2'-fluoro-4'-hydroxy-5'-methoxy-[1,1'-biphenyl]-2-yl)ethan-1-one (**1q**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1/15), white solid (85%). Mp: 155-157 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (dd, J = 7.7, 1.4 Hz, 1H), 7.52 (td, J = 7.5, 1.4 Hz, 1H), 7.46 – 7.33 (m, 2H), 6.78 – 6.69 (m, 2H), 5.88 (d, J = 1.5 Hz, 1H), 3.87 (s, 3H), 2.27 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 203.1, 154.7, 146.4, 143.2, 140.7, 134.2, 131.4, 130.9, 127.8, 127.7, 118.9, 112.4, 103.2, 102.9, 56.5, 29.3. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{15}H_{14}FO_3$ 261.0921; found, 261.0927.

1-(4'-hydroxy-2'-methoxy-[1,1'-biphenyl]-2-yl)ethan-1-one (**1r**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1/15), yellow solid (85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (dd, J = 7.6, 1.4 Hz, 1H), 7.50 (td, J = 7.5, 1.5 Hz, 1H), 7.40 – 7.29 (m, 2H), 7.06 (d, J = 8.2 Hz, 1H), 6.89 (s, 1H), 6.46 – 6.35 (m, 2H), 3.64 (s, 3H), 2.29 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 204.9, 157.7, 156.6, 140.4, 136.8, 131.5, 131.3, 131.2, 127.2, 126.8, 121.5, 107.9, 99.2, 28.9. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{15}H_{15}O_3$ 243.1016; found, 243.1019.

1-(4'-hydroxy-[1,1'-biphenyl]-2-yl)propan-1-one (**1s**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1/15), brown solid (75%). Mp: 100-101 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.41 (m, 2H), 7.38 (d, J = 7.5 Hz, 2H), 7.18 (dt, J = 8.5, 2.0 Hz, 2H), 6.88 (dt, J = 8.5, 2.0 Hz, 2H), 6.43 (d, J = 3.5 Hz, 1H), 2.34 (q, J = 6.4, 5.8 Hz, 2H), 0.94 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 210.7, 156.0, 140.7, 139.8, 130.6, 130.1, 130.1, 127.5, 127.0, 115.8, 36.3, 8.7. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{15}H_{15}O_2$ 227.1067; found, 227.1067.

1-(4'-hydroxy-[1,1'-biphenyl]-2-yl)-4-phenylbutan-1-one (**1t**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1/15), brown oil (65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.40 (m, 2H), 7.34 (q, J = 5.2, 2.8 Hz, 2H), 7.18 (dd, J = 18.7, 11.3 Hz, 5H), 6.98 (d, J = 7.2 Hz, 2H), 6.85 (d, J = 7.6 Hz, 2H), 6.54 (s, 1H), 2.40 (t, J = 6.8 Hz, 2H), 2.32 (t, J = 6.5 Hz, 2H), 1.76 (p, J = 7.7 Hz, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 210.0, 156.1, 141.4, 140.7, 140.0, 132.6, 130.7, 130.2, 130.1, 128.4, 128.4, 127.6, 127.1, 125.9, 115.8, 42.4, 35.0, 26.3. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{22}H_{21}O_2$ 317.1536, found, 317.1538.

1-(4'-hydroxy-[1,1'-biphenyl]-2-yl)-3-(4-methoxyphenyl)propan-1-one (**1u**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1/15), brown solid (50%). Mp: 87-90 °C.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 7.7 Hz, 1H), 7.34 – 7.24 (m, 3H), 7.07 (t, J = 5.5 Hz, 2H), 6.76 (dt, J = 9.4, 5.0 Hz, 4H), 6.65 (dd, J = 8.6, 3.2 Hz, 2H), 5.98 – 5.61 (m, 1H), 3.67 (s, 3H), 2.63 (t, J = 7.5 Hz, 2H), 2.50 (t, J = 7.5 Hz, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 208.4, 157.8, 155.9, 140.7, 139.8, 132.9, 132.8, 130.6, 130.1, 130.1, 129.3, 127.6, 127.1, 115.8, 113.8, 55.3, 45.0, 29.8. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{22}H_{21}O_3$ 333.1485; found, 333.1482.

ethyl 3-(4'-hydroxy-[1,1'-biphenyl]-2-yl)-3-oxopropanoate (**1v**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1/15), brown oil (50%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (dd, J = 7.7, 1.4 Hz, 1H), 7.52 (td, J = 7.5, 1.4 Hz, 1H), 7.42 – 7.36 (m, 2H), 7.19 (d, J = 6.6 Hz, 2H), 6.93 – 6.87 (m, 2H), 4.08 (q, J = 7.1 Hz, 2H), 3.36 (s, 2H), 1.17 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 199.9, 167.6, 156.6, 140.6, 139.1, 131.9, 131.5, 130.4, 130.3, 128.6, 127.1, 116.0, 61.5, 48.7, 13.9.

1-(4-hydroxyphenyl)-2-naphthaldehyde (**1w**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1/15), yellow solid (50%). Mp: 226-231 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.83 (d, J = 5.7 Hz, 2H), 8.06 (dd, J = 8.5, 4.9 Hz, 2H), 7.92 (d, J = 8.6 Hz, 1H), 7.70 (t, J = 7.9 Hz, 2H), 7.57 (ddd, J = 8.2, 6.7, 1.3 Hz, 1H), 7.26 (d, J = 8.1 Hz, 2H), 6.99 (d, J = 7.9 Hz, 2H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 192.6, 158.1, 146.8, 132.7, 131.3, 129.4, 128.8, 128.5, 127.7, 127.6, 1245.0, 122.2, 115.6. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{17}H_{13}O_2$ 249.0910, found, 249.0910.

(Z)-3'-(3-phenylpropylidene)-3'H-spiro[cyclohexane-1,1'-isobenzofuran]-2,5-dien-4-one (**B**). Purification by flash column chromatography (ethyl acetate/petroleum ether, v/v, 1/15), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, J = 7.7 Hz, 1H), 7.35 (t, J = 7.5 Hz, 1H), 7.26 (p, J = 7.3 Hz, 5H), 7.18 (t, J = 7.1 Hz, 1H), 7.00 (d, J = 7.6 Hz, 1H), 6.68 (d, J =

9.7 Hz, 2H), 6.24 (d, J = 9.6 Hz, 2H), 5.09 (t, J = 7.5 Hz, 1H), 2.80 (t, J = 7.5 Hz, 2H), 2.63 (q, J = 7.5 Hz, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 185.3, 153.2, 147.0, 141.9, 138.5, 129.4, 128.9, 128.6, 128.2, 127.6, 125.8, 122.0, 120.4, 97.4, 83.3, 35.9, 26.6. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{17}H_{13}O_2$ 315.1380, found, 315.1378.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

^1H, ^{13}C NMR and HRMS spectra for all compounds (PDF)

AUTHOR INFORMATION

Corresponding Author

*E-mail: wangbin@nankai.edu.cn (B. W.).

ROCID

Bin Wang: 0000-0002-3674-8980

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

Financial support by the National Science Foundation of China (no. 21172120 and 21472093), Tianjin Municipal Science and Technology Commission (No. 19JCTPJC48400) , National University Student Innovation Program (201910055456) and the Fundamental Research Funds for the Central Universities，Nankai University (63201023).

REFERENCES

1. (a) Zhdankin, V. V.; Stang, P. J. Chemistry of Polyvalent Iodine. *Chem. Rev.* **2008,** *108*, 5299-5358; (b) Parra, A.; Reboredo, S. Chiral Hypervalent Iodine Reagents: Synthesis and Reactivity. *Chem. Eur. J.* **2013,** *19*, 17244-17260; (c) Dong, D.-Q.; Hao, S.-H.; Wang, Z.-L.; Chen, C. Hypervalent iodine: a powerful electrophile for asymmetric alpha-functionalization of carbonyl compounds. *Org. Biomol. Chem.* **2014,** *12*, 4278-4289; (d) Yoshimura, A.; Zhdankin, V. V. Advances in Synthetic Applications of Hypervalent Iodine Compounds. *Chem. Rev.* **2016,** *116*, 3328-3435; (e) Li, X.; Chen, P.; Liu, G. Recent advances in hypervalent iodine(III)-catalyzed functionalization of alkenes. *Beilstein J. Org. Chem.* **2018,** *14*, 1813-1825; (f) Lee, J. H.; Choi, S.; Hong, K. B. Alkene difunctionalization using hypervalent iodine reagents: progress and developments in the past ten years. *Molecules* **2019,** *24*, 2634pp.

2. Quideau, S.; Pouysegu, L.; Deffieux, D. Oxidative dearomatization of phenols: Why, how and what for? *Synlett* **2008**, 467-495.

3. (a) Ding, Q.; Ye, Y.; Fan, R. Recent Advances in Phenol Dearomatization and Its Application in Complex Syntheses. *Synthesis* **2013,** *45*, 1-16; (b) Silva, L. F., Jr.; Olofsson, B. Hypervalent iodine reagents in the total synthesis of natural products. *Nat. Prod. Rep.* **2011,** *28*, 1722-1754.

4. (a) Singh, F. V.; Kole, P. B.; Mangaonkar, S. R.; Shetgaonkar, S. E. Synthesis of spirocyclic scaffolds using hypervalent iodine reagents. *Beilstein J. Org. Chem.* **2018,** *14*, 1778-1805; (b) Quideau, S.; Pouysegu, L.; Peixoto, P. A.; Deffieux, D., Phenol Dearomatization with Hypervalent Iodine Reagents. In *Hypervalent Iodine Chemistry*, Wirth, T., Ed. 2016; Vol. 373, pp 25-74.

5. (a) Uyanik, M.; Sasakura, N.; Mizuno, M.; Ishihara, K. Enantioselective Synthesis of Masked Benzoquinones Using Designer Chiral Hypervalent Organoiodine(III) Catalysis. *ACS Cat.* **2017,** *7*, 872-876; (b) Odagi, M.; Okuda, K.; Ishizuka, H.; Adachi, K.; Nagasawa, K. Synthesis of Spiroguanidine Derivatives by Dearomative Oxidative Cyclization using Hypervalent Iodine Reagent. *Asian J. Org. Chem.* **2020,** *9*, 218-221; and references cited therein.

6. CCDC Deposition Number 1972295.

7. Podolesov, B. Oxidation of β-diketones with (diacetoxyiodo)benzene. *J. Org. Chem.* **1984,** *49*, 2644-6.

8. (a) Kang, Y.-B.; Gade, L. H. The Nature of the Catalytically Active Species in Olefin Dioxygenation with PhI(OAc)2: Metal or Proton? *J. Am. Chem. Soc.* **2011,** *133*, 3658-3667; (b) Xu, J.-H.; Jiang, Q.; Guo, C.-C. Phenyliodonium Diacetate Mediated Direct Synthesis of Benzonitriles from Styrenes through Oxidative Cleavage of C═C Bonds. *J. Org. Chem.* **2013,** *78*, 11881-11886.

9. Li, Y.; Song, D.; Dong, V. M. Palladium-Catalyzed Olefin Dioxygenation. *J. Am. Chem. Soc.* **2008,** *130*, 2962-2964.

10. (a) Nicolaou, K. C.; Adsool, V. A.; Hale, C. R. H. An Expedient Procedure for the Oxidative Cleavage of Olefinic Bonds with PhI(OAc)2, NMO, and Catalytic OsO_4. *Org. Lett.* **2010,** *12*, 1552-1555; (b) Hong, Z.; Liu, L.; Sugiyama, M.; Fu, Y.; Wong, C.-H. Concise Synthesis of Iminocyclitols via Petasis-Type Aminocyclization. *J. Am. Chem. Soc.* **2009,** *131*, 8352-8353; (c) Ohno, M.; Oguri, I.; Eguchi, S. PhI(OAc)2-Promoted Rearrangement of the Hydroxyl Group: Ring Expansion of 4-Hydroxy-2-cyclobutenone to 2(5H)-Furanone in Comparison with Ring Cleavage of the α-Hydroxycycloalkanone to the ω-Formyl Ester. *J. Org. Chem.* **1999,** *64*, 8995-9000; (d) Moorthy, J. N.; Parida, K. N. Oxidative Cleavage of Olefins by In Situ-Generated Catalytic 3,4,5,6-Tetramethyl-2-iodoxybenzoic Acid/Oxone. *J. Org. Chem.* **2014,** *79*, 11431-11439; (e) Miyamoto, K.; Yamashita, J.; Narita, S.; Sakai, Y.; Hirano, K.; Saito, T.; Wang, C.; Ochiai, M.; Uchiyama, M. Iodoarene-catalyzed oxidative transformations using molecular oxygen. *Chem. Commun.* **2017,** *53*, 9781-9784.

11. (a) Jiang, Y. T.; Yu, Z. Z.; Zhang, Y. K.; Wang, B. N-Bromosuccinimide-Induced C-H Bond Functionalization: An Intramolecular Cycloaromatization of Electron Withdrawing Group Substituted 1-Biphenyl-2-ylethanone for the Synthesis of 10-Phenanthrenol. *Org. Lett.* **2018,** *20*, 3728-3731; (b) Tang, C.; Yuan, Y.; Jiao, N. Metal-Free Nitrogenation of 2-Acetylbiphenyls: Expeditious Synthesis of Phenanthridines. *Org. Lett.* **2015,** *17*, 2206-2209.

12. Dohi, T.; Maruyama, A.; Yoshimura, M.; Morimoto, K.; Tohma, H.; Kita, Y. Versatile hypervalent-iodine(III)-catalyzed oxidations with m-chloroperbenzoic acid as a cooxidant. *Angew. Chem., Int. Ed.* **2005,** *44*, 6193-6196.

13. Hart, D. J.; Kim, A.; Krishnamurthy, R.; Merriman, G. H.; Waltos, A.-M. Synthesis of 6H-dibenzo[b,d]pyran-6-ones via dienone-phenol rearrangements of spiro[2,5-cyclohexadiene-1,1′(3′H)-isobenzofuran]-3′-ones. *Tetrahedron* **1992,** *48*, 8179-8188.

14. Li, H.; Subbotina, E.; Bunrit, A.; Wang, F.; Samec, J. S. M. Functionalized spirolactones by photoinduced dearomatization of biaryl compounds. *Chem. Sci.* **2019,** *10*, 3681-3686.

15. Aparece, M. D.; Vadola, P. A. Gold-Catalyzed Dearomative Spirocyclization of Aryl Alkynoate Esters. *Org. Lett.* **2014,** *16*, 6008-6011.

16. Bao, H.; Xu, Z.; Wu, D.; Zhang, H.; Jin, H.; Liu, Y. Copper(0)/Selectfluor System-Promoted Oxidative Carbon–Carbon Bond Cleavage/Annulation of o-Aryl Chalcones: An Unexpected Synthesis of 9,10-Phenanthraquinone Derivatives. *J. Org. Chem.* **2017,** *82*, 109-118.