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PAPER

New fluoride-promoted hypoiodite-catalytic oxidative cycloetherification to aromatic spiroketals†

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A new catalytic application of hypoiodite reagents generated *in situ* from iodide ions is found, which succeeded in the synthesis of bisbenzannelated spiroketal cores for the first time. Fluoride was proven to be obligatory for this spiroketalization, which is the first fluoride-promoted oxidative cycloetherification to aromatic spiroketals.

Introduction

Organohypervalent iodine reagents have attracted significant recent interest as versatile and environmentally benign oxidants with many applications in organic synthesis.[1] The most impressive recent achievements in this field include the development of new hypervalent iodine reagents and reagent systems and the discovery of catalytic applications of organoiodine compounds.[2] In 2005, Ochiai and co-workers reported the first PhI catalyzed reaction.[3] Since then, several other reactions based on the generation of iodine(III) species have been reported.[1b,c,4] However, most of the hypervalent species generated from iodoarenes. In 2010, Ishihara and co-workers reported the chiral quaternary ammonium iodide catalyst for oxidative cycloetherification of ketophenol[4b] and subsequently an intramolecular and intermolecular oxidative coupling reactions of carbonyl compounds with carboxylic acids catalyzed by *in situ* generated tetrabutylammonium hypoiodite.[5] These are the only cases using organoiodide salts as the sources of hypervalent iodite, which is a new organoiodine species with very high application potency, so exploring more new iodide catalysts and developing their applications are necessary and significant.

Significant attention is currently being paid to the applications of hypervalent iodine is α-oxyacetylation and α-oxyalkylation of carbonyl compounds to construct lactones, pyrans, furans, and even aliphatic spiroketal or spirolactone cores.[6] However, to the best of our knowledge, there is only one report on α-oxyphenylation and no reports on the catalytic application of organoiodide on the construction of bisbenzannelated spiroketal cores. As a fundamental building block of synthetic organic chemistry, spiroketal cores widely exist in natural and unnatural bioactive compounds, such as lyscidicins, pinnatifinosides, berkelic acid, rubromycin family (Fig. 1), *etc*.[7,8] They play important roles in the structure–activity relationship. There is a strong requirement for developing some novel mild spirocyclisation methodologies, which can be widely employed, for the traditional methods are limited by the scope of its substrate and less efficient multi-steps conversion.

Results and discussion

During our investigation[9] of the synthesis of rubromycin families, intramolecular α-oxyphenylation of carbonyl compounds catalyzed by tetrabutylammonium iodide in the presence of oxidants was proposed to constitute the spiroketal cores and an approach *via* a hypoiodite system was found, which includes a fluoride reagent as a promoting reagent and organoiodide salts as the source of hypoiodite.

The investigation was initialized from the cyclization of compound **1a**. To our delight, bisbenzannulated spiroketals **2a** formed smoothly from compound **1a** in the presence of TBAI and *m*-chlorobenzoic acid (*m*CPBA) in THF as solvent. Initially, compound **1a** was treated with TBAI and *m*CPBA in THF. In 0.5 h, a trace of **2a** was found when 5 mol% TBAI and 2.0 eq. *m*CPBA were used (Table 1, entry 1). The yield increased to 42% when TBAI increased to 15 mol% (Table 1, entry 2). To our surprise, a significant increase in yield was observed when TBAF was introduced to the system. 20 mol% TBAF, 15 mol%

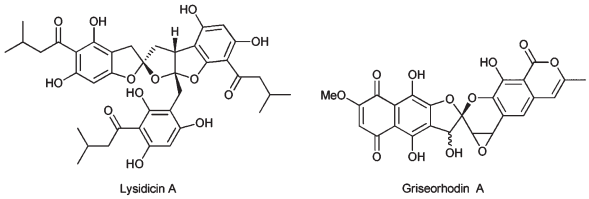

Fig. 1 Benzannulated spiroketal natural products.

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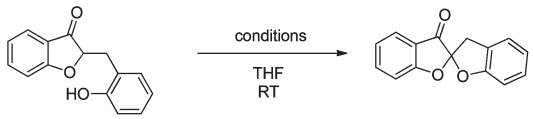
Table 1 Optimization of the reaction conditions

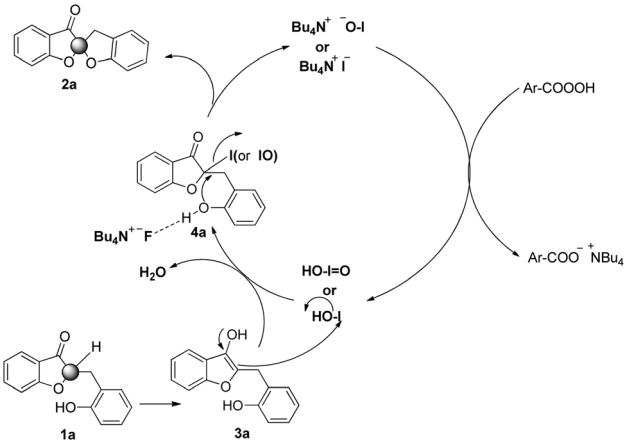


Entry	Oxidant[a]	Additive (eq.)	Reaction time	TBAI (mol%)	Yield (%)
1	*m*CPBA	None	0.5 h	5	Trace
2	*m*CPBA	None	0.5 h	15	42
3	*m*CPBA	TBAF (0.2)	0.5 h	15	56
4	*m*CPBA	TBAF (1.0)	5 min	15	77
5	*m*CPBA	TBAF (2.0)	5 min	15	89
6	*m*CPBA	KF (2.0)	5 min	15	Trace
7	*m*CPBA	KF (2.0) 18-crown-6 (2.0)	5 min	15	71[b]
8	*m*CPBA	$NaHCO_3$ (2.0)	5 min	15	Trace
9	*m*CPBA	Imidazole (2.0)	5 min	15	13
10	TBHP	TBAF (2.0)	5 min	15	63
11	H_2O_2	TBAF (2.0)	5 min	15	68

[a] The dosage of oxidant is 2.0 equivalent. [b] The procedure see ref. 12.

TBAI and 2.0 eq. *m*CPBA gave **2a** in 56% yield (Table 1, entry 3). 77% and 89% yield of **1a** formed in only 5 minutes when 1.0 eq. and 2.0 eq. of TBAF were used, respectively (Table 1, entries 4, 5). When TBHP or H_2O_2 took the place of *m*CPBA, the yield decreased slightly (Table 1, entries 10 and 11). So a new condition was found for the α-oxyphenylation of ketone to construct spiroketal **2a**: 2.0 eq. of TBAF as additive, 15 mol% of TBAI as catalyst source, and 2.0 eq. of *m*CPBA as oxidant were stirred at room temperature with **1a** in THF as solvent in 5 minutes (Table 1, entry 5).

Now it is necessary to make clear the role of TBAF. Another potential fluoride source, potassium fluoride, was used to take the place of TBAF. However, it does not seem to benefit the reaction (Table 1, entry 6). Considering the solubility, 18-crown-6 was added to the reaction as a phase transfer catalyst to increase the solubility of KF, and it apparently increase the yield to 71% (Table 1, entry 7). These controlled experiments show that fluoride is obligatory for the transformation and it is responsible for the increasing of the yield. A detailed review of organofluoride chemistry shows that fluoride was mainly used as a base and an activator of C–Si bonds for oxidation.[10] Much research also shows the significant role of fluoride ion in varied oxidations, especially the oxidative nucleophilic aromatic substitution of hydrogen. In 2001, Marquet and co-workers[11] reported direct coupling of nucleophiles with nitro aromatic compounds *via* fluoride-promoted oxidative nucleophilic aromatic substitution for hydrogen. However, there is still no report on the detailed explanation of the role of fluoride. We hypothesized that fluoride in this present spiroketalization maybe take as a hydrogen-bond acceptor to increase the nucleophilicity of aromatic hydroxyl group of **1a** and accelerate the spiroketalization (Scheme 1). Fluoride is not easily oxidized and can form very strong hydrogen bonds, even with hydrogen bonded to carbon. In the spiroketalization of **1a**, fluoride may bond to H–O on aromatic ring of **4a**, which may increase the nucleophilicity of OH group and accelerate the cycloetherification. At the same time



Scheme 1 The proposed catalytic cycle.

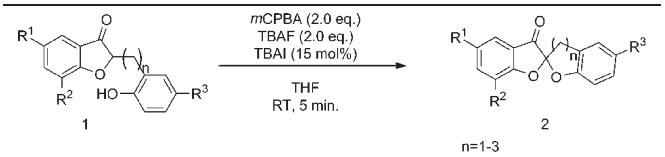
fluoride partially transfer negative charge upon hydrogen bond formation, which made the oxidation tendency of hydrogen-bonded-complex lower than the free anion of substrate and increase the selectivity and yield of oxidative nucleophilic substitution.

According to the literature,[3,4b] it is clear that TBAI can be oxidized to iodite(I) or iodite(III) and will be reduced to iodide or iodite(I) in reactions, based on which a catalytic cycle was hypothesized as Scheme 1. The reaction of *m*CPBA and TBAI formed iodous acid or hypoiodous acid, which reacted as an electrophile with the double bond of **3a** obtained from the enolization of **1a**, and formed iodo or hypoiodo substituted **4a**. A similar process has been reported by Ochiai and Kita.[3] The followed S_N1 displacement of iodo or hypoiodo group in **1a** by phenolic hydroxyl group activated by hydrogen bond with fluoride affords spiroketal **2a**. During this process, when bases were used to take the place of fluoride reagent (Table 1, entries 8, 9), less efficient results were observed, for iodous acid or hypoiodous acid reacted with bases and formed iodite salt or hypoiodite salt which has no electrophilicity.

Based on the above modified conditions, more substrates were screened with different substituted **1** and the corresponding yields of spiroketals ranged from good to excellent within a short period of time and [5,5], [5,6] even [5,7] spiroketal cores were obtained. Compared to the formation of [5,5] spiroketals, the formation of [5,6] and [5,7] spiroketals take longer times and was slightly less efficiency. The reaction of **1a** gave 89% yield of **2a** in 5 minutes (Table 2, entry 1). However in 5 minutes, **2l** and **2m** formed from **1l** (Table 2, entry 12) and **1m** (Table 2, entry 14) in only 27% and 17% yields, respectively. After 12 hours, the yields of **2l** and **2m** just reach to 62% and 43% (Table 2, entries 13, 15), which are much lower than that of **2a**. So it could be concluded that this reaction favored the formation of smaller rings.

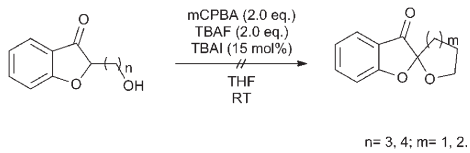
In the formation of [5,5] spiroketals, all cases gave very excellent results. However, a slightly different electron effect is shown between the two aromatic rings. The electron effects of substitutions on the right aromatic ring have more obvious effect than that on the left ring. For the left benzofuranone, electron-donating group on R^1 or R^2 position will decrease the efficiency of spiroketalization. When R^1 or R^2 is methoxyl group, the

Table 2 Synthesis of [5,X] spiroketals with α-oxyphenylation of carbonyl compounds



Entry	N	R^1	R^2	R^3	Products	Yield[ab] (%)
1	1 (**1a**)	H	H	H	**2a**	89
2	1 (**1b**)	H	H	Me	**2b**	81
3	1 (**1c**)	H	H	MeO	**2c**	76
4	1 (**1d**)	H	H	Br	**2d**	92
5	1 (**1e**)	H	H	COOEt	**2e**	87
6	1 (**1f**)	H	MeO	Br	**2f**	82
7	1 (**1g**)	H	MeO	COOEt	**2g**	88
8	1 (**1h**)	MeO	H	Br	**2h**	83
9	1 (**1i**)	MeO	H	COOEt	**2i**	85
10	1 (**1j**)	Br	H	Br	**2j**	86
11	1 (**1k**)	Br	H	COOEt	**2k**	84
12	2 (**1l**)	H	H	H	**2l**	27
13	2 (**1l**)	H	H	H	**2l**	62[a]
14	3 (**1m**)	H	H	H	**2m**	17
15	3 (**1m**)	H	H	H	**2m**	43[a]
16	1 (**1c**)	H	H	MeO	**2c**	87[b]
17	3 (**1m**)	H	H	H	**2m**	48[ab]

[a] The reaction time was increased to 12 hours. [b] The dosage of TBAI was increased to 30 mol%.



Scheme 2 The cycloetherification of aliphatic OH group.

corresponding yield of spiroketal is slightly lower than that R^1 or R^2 is hydrogen. When R^1 or R^2 is bromide, no obvious effect was observed. Whereas R^3 is electron-donating group, such as methyl or methoxyl group, obvious decreases of yields were found and electron withdrawing R^3 (Table 2, entries 5, 7, 9, and 11) gave a much better yield than electron donating ones (Table 2, entries 2, 3).

Moreover, increasing the dosage of iodide will increase the yield, too. When TBAI increased from 15 mol% to 30 mol%, the yield of **1c** also increased from 76% to 87% (Table 2, entries 3, 16). From Table 1, we know that increase of TBAF can increase the yield, too. Hence, higher efficiency of this transformation can be obtained from the larger dosage of reagents.

As a comparison to the present similar transformation,[3] as well as to make clear the role of fluoride, some controlled experiments were done with ketoalcohols. As shown in Scheme 2, these conditions appear to prefer the oxidative nucleophile substitution of the phenolic hydroxyl group rather than the alcohols'. This may be because the iodo group is on a tertiary carbon of **4a** and the cyclization reaction of **4a** is an intramolecular S_N1 displacement. Phenol is favored for S_N1 reaction as a nucleophilic reagent, but the aliphatic OH group, especially primary alcohol, is favored for S_N2 reaction.

Conclusions

In summary, a new catalytic application of hypoiodite reagents generated *in situ* from TBAI, an easily available organoiodide source, was found in the construction of bisbenzannelated spiroketal cores. Using this hypoiodite, a series of spiroketals were synthesized efficiently, which is the first report on the transformation using a hypoiodite reagent as catalyst. At the same time, fluoride was found to be obligatory for this cycloetherification as an activator of S_N1 displacement, which is the first case using fluoride to activate the oxidative cycloetherification to aromatic spiroketals. This work also showed high potency in the stereoselective synthesis of enantiomeric spiroketals, the main challenge for the synthesis of natural products like rubromycins, for chiral hypoiodite compounds generated from chiral tetraalkylammonium iodide and oxidants have proven to be efficient for the enantiomeric α-oxyalkylation.[4b] So the spiroketalization system, in this context, is a high potential approach for the synthesis of enantiomeric natural spiroketal products, the explorations of which are under way in our laboratory.

Experimental

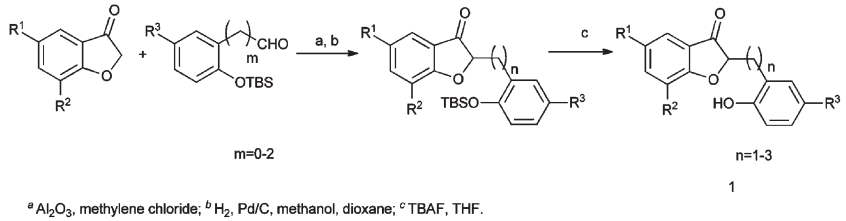
Materials

All reactions under standard conditions were monitored by thin-layer chromatography (TLC) on GF254 plates. The silica gel (200–300 meshes) was used for column chromatography, and the distillation range of petroleum ether was 60–90 °C. THF was dried by distillation over Na–K alloy. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 solution on Bruker AX-400 MHz instruments and spectral data were reported in ppm relative to tetramethylsilane (TMS) as internal standard. Mass spectra (MS) were measured on spectrometer by direct inlet at 70 eV and signals were given in *m*/*z* with relative intensity (%) in brackets. High-resolution mass spectral analysis (HRMS) data were measured on the Bruker Apex II by means of the ESI technique.

Synthesis of starting materials

Known compounds **1a**, **1b**, **1d–1k**[13] and new compounds **1c**, **1l**, **1m** were prepared following the known procedure (Scheme 3).[9a,14]

2-(2-Hydroxy-5-methoxybenzyl)benzofuran-3(2*H*)-one (1c). **^1H NMR** (400 MHz, DMSO-d_6, ppm): δ 9.09 (s, 1H), 7.71 (m, 1H), 7.65 (dd, 1H, J_1 = 0.8 Hz, J_2 = 8.0 Hz), 7.25 (d, 1H, J = 8.4 Hz), 7.13 (m, 1H), 6.73–6.76 (m, 2H), 6.66 (dd, 2H, J_1 = 3.2 Hz, J_2 = 8.8 Hz), 5.06 (dd, 1H, J_1 = 4.0 Hz, J_2 = 10.0 Hz), 3.64 (s, 1H), 3.20 (dd, 1H, J_1 = 3.6 Hz, J_2 = 14.4 Hz), 2.72 (dd, 1H, J_1 = 10.0 Hz, J_2 = 14.4 Hz); **^{13}C NMR** (100 MHz, DMSO-d_6, ppm): δ 200.70, 171.93, 151.86, 149.21, 138.25, 123.91, 123.53, 121.95, 120.47, 116.63, 115.33, 113.62, 112.56, 84.16, 55.26, 31.73; **IR** (KBr, cm^{-1}): 3369, 2926, 2853, 2837, 1818, 1704, 1609, 1460, 1216, 1147, 857, 795, 751; **HRMS** (ESI): Calcd For $C_{16}H_{15}O_4^+$ $[M + H]^+$: 271.0965, found 271.0961.



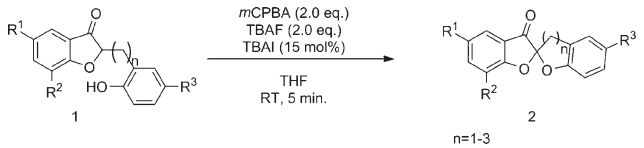
[a] Al_2O_3, methylene chloride; [b] H_2, Pd/C, methanol, dioxane; [c] TBAF, THF.

Scheme 3 Synthesis of compound **1**.

2-(2-Hydroxyphenethyl)benzofuran-3(2*H*)-one (1l). **^{1}H NMR** (400 MHz, DMSO-d_6, ppm): δ 9.38 (s, 1H), 7.72–7.74 (m, 1H), 7.62–7.64 (m, 1H), 7.31 (d, 1H, J = 8.4 Hz), 7.15 (t, 1H, J = 7.2 Hz), 6.99–7.05 (m, 2H), 6.78 (d, 1H, J = 7.6 Hz), 6.70 (t, 1H, J = 7.2 Hz), 4.75 (dd, 1H, J_1 = 4.0 Hz, J_2 = 8.4 Hz), 2.66–2.70 (m, 2H), 2.13–2.18 (m, 2H), 1.86–1.91 (m, 1H); **^{13}C NMR** (100 MHz, DMSO-d_6, ppm): δ 201.30, 172.07, 155.20, 138.37, 129.90, 127.26, 126.69, 123.90, 122.02, 120.67, 118.98, 114.96, 113.59, 84.69, 30.85, 25.41; **IR** (KBr, cm^{-1}): 3431, 2926, 2853, 1726, 1605, 1460, 1279, 1128, 747; **HRMS** (ESI): Calcd For $C_{16}H_{14}O_3Na^+$ $[M + Na]^+$: 277.0835, found 277.0832.

2-(3-(2-Hydroxyphenyl)propyl)benzofuran-3(2*H*)-one (1m). **^{1}H NMR** (400 MHz, DMSO-d_6, ppm): δ 9.21 (s, 1H), 7.71 (m, 1H), 7.62 (d, 1H, J = 7.6 Hz), 7.27 (d, 1H, J = 7.6 Hz), 7.13 (t, 1H, J = 7.2 Hz), 6.96–7.02 (m, 2H), 6.76 (d, 1H, J = 8.0 Hz), 6.68 (t, 1H, J = 7.6 Hz), 4.82 (dd, 1H, J_1 = 4.0 Hz, J_2 = 7.6 Hz), 2.53–2.57 (m, 2H), 1.83–1.93 (m, 1H), 1.58–1.73 (m, 3H); **^{13}C NMR** (100 MHz, DMSO-d_6, ppm): δ 201.39, 172.04, 155.03, 138.31, 129.86, 127.63, 126.85, 123.78, 121.93, 120.63, 118.82, 114.89, 113.46, 84.90, 30.46, 29.26, 24.50; **IR** (KBr, cm^{-1}): 3435, 2932, 2863, 1726, 1601, 1466, 1279, 1132, 751; **HRMS** (ESI): Calcd For $C_{17}H_{17}O_3^+$ $[M + H]^+$: 269.1172, found 269.1168.

Synthesis of [5,X] spiroketalswith α-oxyphenylation of carbonyl compounds



3*H*,3′*H*-2,2′-Spirobi[benzofuran]-3-one (2a). TBAI 5 mg (15 mol%) was added to a stirring solution of compound **1a** 24 mg (0.1 mmol) in 5 mL THF and then the solution of *m*CPBA 20 mg (2.0 eq.) and TBAF 32 mg (2.0 eq.) in 5 mL THF at room temperature was added dropwise in 5 min. The resulting solution was quenched with water, extracted (DCM), washed with Na_2SO_3, $NaHCO_3$ and brine, dried with Na_2SO_4, filtered, and concentrated. Chromatography on silica gel (petroleum ether–EtOAc 16 : 1, v/v) of the crude product afforded **2a** (89%) as a solid, m.p.: 117–118 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.73 (d, 1H, J = 7.6 Hz), 7.66 (m, 1H), 7.21 (t, 1H, J = 8.0 Hz), 7.14 (t, 1H, J = 7.6 Hz), 7.07 (d, 1H, J = 8.4 Hz), 7.00 (t, 1H, J = 7.6 Hz), 6.93 (d, 1H, J = 8.0 Hz), 3.67 (d, 1H, J = 17.2 Hz), 3.39 (d, 1H, J = 16.8 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 195.76, 170.49, 157.61, 139.36, 128.58, 125.23, 124.82, 123.88, 122.93, 122.40, 118.82, 113.33, 110.54, 110.19, 37.82; **IR** (KBr, cm^{-1}): 2926, 2853, 1720, 1600, 1475, 1460, 1325, 1220, 750; **HRMS** (ESI): Calcd For $C_{15}H_{11}O_3^+$ $[M + H]^+$: 239.0703, found 239.0701.

5′-Methyl-3*H*,3′*H*-2,2′-spirobi[benzofuran]-3-one (2b). Following the procedure of **2a**, the reaction gives **2b** (81%) as a solid, m.p.: 105–106 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.74 (d, 1H, J = 0.8 Hz), 7.67 (m, 1H), 7.14 (t, 1H, J = 7.6 Hz), 7.10 (s, 1H), 7.06 (d, 1H, J = 8.4 Hz), 7.01 (t, 1H, J = 8.0 Hz), 6.82 (d, 1H, J = 8.4 Hz), 3.65 (d, 1H, J = 16.8 Hz), 3.36 (d, 1H, J = 16.8 Hz), 2.33 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 195.83, 170.50, 155.62, 139.29, 131.85, 128.93, 125.35, 125.20, 123.85, 122.85, 118.89, 113.33, 110.82, 109.69, 37.36, 20.84; **IR** (KBr, cm^{-1}): 3390, 2926, 2853, 1725, 1610, 1465, 1460, 1325, 1200, 880, 860, 760; **HRMS** (ESI): Calcd For $C_{16}H_{13}O_3^+$ $[M + H]^+$: 253.0859, found 253.0864.

5′-Methoxy-3*H*,3′*H*-2,2′-spirobi[benzofuran]-3-one (2c). Following the procedure of **2a**, the reaction gives **2c** (76%) as a solid, m.p.: 117–119 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.71–7.65 (m, 2H), 7.14 (m, 1H), 7.06 (d, 1H, J = 8.4 Hz), 6.86 (m, 2H), 6.75 (dd, 1H, J_1 = 2.8 Hz, J_2 = 8.8 Hz), 3.78 (s, 3H), 3.67 (d, 1H, J = 16.8 Hz), 3.36 (d, 1H, J = 16.8 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 195.64, 170.45, 155.56, 151.70, 139.31, 125.19, 124.87, 122.85, 118.83, 113.58, 113.31, 111.02, 110.95, 110.18, 55.98, 37.72; **IR** (KBr, cm^{-1}): 2926, 2853, 2850, 1730, 1605, 1480, 1460, 1405, 1290, 875, 805, 730; **HRMS** (ESI): Calcd For $C_{16}H_{13}O_4^+$ $[M + H]^+$: 269.0808, found 269.0813.

5′-Bromo-3*H*,3′*H*-2,2′-spirobi[benzofuran]-3-one (2d). Following the procedure of **2a**, the reaction gives **2d** (92%) as a solid, m.p.: 111–112 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.67–7.72 (m, 2H), 7.41 (s, 1H), 7.34 (dd, 1H, J_1 = 0.8 Hz, J_2 = 8.4 Hz), 7.17 (t, 1H, J = 7.2 Hz), 7.09 (d, 1H, J = 8.4 Hz), 6.82 (d, 1H, J = 8.4 Hz), 3.68 (d, 1H, J = 17.2 Hz), 3.40 (d, 1H, J = 16.8 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 195.03, 170.39, 156.80, 139.46, 131.44, 127.83, 126.40, 125.30, 123.12, 118.63, 114.46, 113.29, 111.65, 110.63, 36.96; **IR** (KBr, cm^{-1}): 2926, 2853, 1737, 1612, 1460, 1458, 1414, 1246, 910, 820, 754, 527; **HRMS** (ESI): Calcd For $C_{15}H_{13}BrNO_3^+$ $[M + NH_4]^+$: 334.0073, found 334.0075.

Ethyl 3′-oxo-3*H*,3′*H*-2,2′-spirobi[benzofuran]-5-carboxylate (2e). Following the procedure of **2a**, the reaction gives **2e** (87%) as oil. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.99–8.01 (m, 2H), 7.74 (d, 1H, J = 7.2 Hz), 7.34 (m, 1H), 7.18 (t, 1H, J = 7.2 Hz), 7.09 (d, 1H, J = 8.4 Hz), 6.96 (d, 1H, J = 8.4 Hz), 4.37 (q, 2H, J = 7.2 Hz), 3.70 (d, 1H, J = 16.8 Hz), 3.45 (d, 1H, J = 16.8

Hz), 1.39 (t, 3H, J = 7.2 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 195.01, 170.41, 166.08, 161.22, 139.50, 131.34, 126.59, 125.34, 125.12, 124.46, 123.20, 118.60, 113.30, 110.84, 109.82, 60.86, 36.53, 14.33; **IR** (KBr, cm^{-1}): 2984, 2926, 2907, 2853, 1719, 1664, 1616, 1460, 1447, 1440, 1436, 1257, 1249, 1154, 905, 864, 758; **HRMS** (ESI): Calcd For $C_{18}H_{15}O_5^+$ $[M + H]^+$: 311.0914, found 311.0917.

5′-Bromo-7-methoxy-3*H*,3′*H*-2,2′-spirobi[benzofuran]-3-one (2f). Following the procedure of **2a**, the reaction gives **2f** (82%) as a solid, m.p.: 136–137 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.37 (s, 1H), 7.29 (m, 2H), 7.19 (d, 1H, J = 7.6 Hz), 7.09 (t, 1H, J = 7.8 Hz), 6.79 (d, 1H, J = 8.4 Hz), 3.92 (s, 3H), 3.68 (d, 1H, J = 17.2 Hz), 3.45 (d, 1H, J = 16.8 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 195.09, 160.22, 156.77, 145.97, 131.28, 127.69, 126.33, 123.56, 120.12, 119.52, 116.08, 114.37, 111.63, 110.84, 56.15, 37.03; **IR** (KBr, cm^{-1}): 2926, 2853, 2582, 1854, 1733, 1605, 1460, 1279, 1158, 864, 808, 738, 523; **HRMS** (ESI): Calcd For $C_{16}H_{12}BrO_4^+$ $[M + H]^+$: 346.9913, found 346.9916.

Ethyl 7′-methoxy-3′-oxo-3*H*,3′*H*-2,2′-spirobi[benzofuran]-5-carboxylate (2g). Following the procedure of **2a**, the reaction gives **2g** (88%) as oil. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.99 (s, 1H), 7.97 (s, 1H), 7.33 (dd, 1H, J_1 = 7.6 Hz, J_2 = 0.8 Hz), 7.21 (d, 1H, J = 7.2 Hz), 7.12 (t, 1H, J = 7.6 Hz), 6.95 (d, 1H, J = 8.4 Hz), 4.36 (q, 2H, J = 7.2 Hz), 3.95 (s, 3H), 3.71 (d, 1H, J = 17.2 Hz), 3.51 (d, 1H, J = 16.8 Hz), 1.40 (t, 3H, J = 7.2 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 195.15, 166.11, 161.26, 160.30, 146.03, 131.26, 126.53, 125.06, 124.44, 123.70, 120.21, 119.59, 116.22, 111.09, 109.88, 60.86, 56.24, 36.68, 14.31; **IR** (KBr, cm^{-1}): 2962, 2926, 2872, 2853, 1920, 1735, 1715, 1704, 1460, 1375, 1282, 1279, 1158, 1092, 879, 809, 743; **HRMS** (ESI): Calcd For $C_{19}H_{17}O_6^+$ $[M + H]^+$: 341.1020, found 341.1025.

5′-Bromo-5-methoxy-3*H*,3′*H*-2,2′-spirobi[benzofuran]-3-one (2h). Following the procedure for **2a**, the reaction gives **2h** (83%) as a solid, m.p.: 129–131 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.39 (s, 1H), 7.28–7.33 (m, 2H), 7.11 (d, 1H, J = 2.8 Hz), 7.00 (d, 1H, J = 8.8 Hz), 6.80 (d, 1H, J = 8.4 Hz), 3.81 (s, 1H), 3.66 (d, 1H, J = 17.2 Hz), 3.38 (d, 1H, J = 16.8 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 195.31, 165.63, 156.75, 155.63, 131.34, 129.03, 127.77, 126.41, 118.45, 114.35, 114.17, 111.58, 111.27, 105.17, 55.89, 36.99; **IR** (KBr, cm^{-1}): 2926, 2853, 1848, 1876, 1737, 1711, 1460, 1275, 1161, 809, 747, 534; **HRMS** (ESI): Calcd For $C_{16}H_{12}BrO_4^+$ $[M + H]^+$: 346.9913, found 346.9909.

Ethyl 5′-methoxy-3′-oxo-3*H*,3′*H*-2,2′-spirobi[benzofuran]-5-carboxylate (2i). Following the procedure of **2a**, the reaction gives **2i** (85%) as oil. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 8.00 (s, 1H), 7.98 (s, 1H), 7.31 (dd, 1H, J_1 = 9.2 Hz, J_2 = 2.8 Hz), 7.13 (d, 1H, J = 2.4 Hz), 7.02 (d, 1H, J = 8.8 Hz), 6.96 (d, 1H, J = 8.0 Hz), 4.37 (q, 2H, J = 7.2 Hz), 3.83 (s, 3H), 3.69 (d, 1H, J = 16.8 Hz), 3.44 (d, 1H, J = 17.2 Hz), 1.39 (t, 3H, J = 7.2 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 195.37, 166.11, 165.73, 161.25, 155.76, 131.32, 129.13, 126.58, 125.04, 124.51, 118.50, 114.24, 111.54, 109.82, 105.26, 60.86, 55.97, 36.62, 14.33; **IR** (KBr, cm^{-1}): 2962, 2926, 2872, 2853, 2844, 1917, 1737, 1708, 1460, 1375, 1279, 1165, 861, 828, 762; **HRMS** (ESI): Calcd For $C_{19}H_{20}NO_6^+$ $[M + NH_4]^+$: 358.1285, found 358.1279.

5,5′-Dibromo-3*H*,3′*H*-2,2′-spirobi[benzofuran]-3-one (2j). Following the procedure of **2a**, the reaction gives **2j** (86%) as a solid, m.p.: 146–147 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.84 (d, 1H, J = 2.0 Hz), 7.76 (dd, 1H, J_1 = 8.8 Hz, J_2 = 2.0 Hz), 7.40 (s, 1H), 7.34 (d, 1H, J = 8.8 Hz), 6.99 (d, 1H, J = 8.8 Hz), 6.81 (d, 1H, J = 8.4 Hz), 3.67 (d, 1H, J = 17.2 Hz), 3.40 (d, 1H, J = 16.8 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 193.77, 169.08, 156.61, 141.94, 131.56, 127.84, 127.76, 126.09, 120.27, 115.63, 115.10, 114.67, 111.69, 111.14, 37.03; **MS** (EI) m/z (%): 398 (M^+ + 4, 3), 396 (M^+ + 2, 7), 394 (M^+, 3), 211 (11), 205 (11), 200 (19), 198 (26), 169 (13), 165 (10), 155 (15), 149 (31), 141 (27), 139 (35), 127 (24), 113 (32), 112 (12), 111 (26), 99 (33), 85 (71), 71 (91), 57 (100), 43 (63); **IR** (KBr, cm^{-1}): 2926, 2853, 1737, 1665, 1460, 1425, 1275, 1161, 846, 809, 765, 490.

Ethyl 5′-bromo-3′-oxo-3*H*,3′*H*-2,2′-spirobi[benzofuran]-5-carboxylate (2k). Following the procedure of **2a**, the reaction gives **2k** (84%) as oil. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 8.01 (s, 1H), 7.99 (s, 1H), 7.85 (d, 1H, J = 2.0 Hz), 7.77 (dd, 1H, J_1 = 8.8 Hz, J_2 = 2.4 Hz), 7.00 (d, 1H, J = 8.8 Hz), 6.95 (d, 1H, J = 9.2 Hz), 4.37 (q, 2H, J = 7.2 Hz), 3.69 (d, 1H, J = 17.2 Hz), 3.44 (d, 1H, J = 17.2 Hz), 1.39 (t, 3H, J = 7.2 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 193.68, 169.13, 166.00, 161.05, 141.94, 131.44, 127.83, 126.61, 125.38, 124.22, 120.33, 115.73, 115.10, 111.38, 109.87, 60.90, 36.62, 14.34; **IR** (KBr, cm^{-1}): 2962, 2926, 2872, 2853, 1891, 1748, 1719, 1460, 1375, 1253, 1161, 861, 828, 758, 516; **HRMS** (ESI): Calcd For $C_{18}H_{14}BrO_5^+$ $[M + H]^+$: 389.0019, found 389.0005.

3*H*-Spiro[benzofuran-2,2′-chroman]-3-one (2l). Following the procedure of **2a**, the reaction gives **2l** (27%) as oil. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.67–7.63 (m, 2H), 7.15 (m, 3H), 7.06 (d, 1H, J = 8.4 Hz), 6.96 (m, 1H), 6.87 (d, 1H, J = 1.2 Hz), 3.23–3.14 (m, 1H), 2.94 (m, 1H), 2.28 (m, 1H), 2.05 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 195.73, 170.50, 151.92, 139.05, 129.19, 127.77, 125.44, 122.60, 122.04, 121.04, 118.93, 117.12, 113.54, 102.35, 25.49, 20.45; **IR** (KBr, cm^{-1}): 2926, 2853, 1726, 1616, 1460, 1436, 1227, 1158, 751; **HRMS** (ESI): Calcd For $C_{16}H_{13}O_3^+$ $[M + H]^+$: 253.0859, found 253.0864.

4,5-Dihydro-3*H*,3′*H*-spiro[benzo[*b*]oxepine-2,2′-benzofuran]-3′-one (2m). Following the procedure of **2a**, the reaction gives **2m** (17%) as oil. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.74 (m, 1H,), 7.62 (m, 1H), 7.19–6.87 (m, 6H), 3.17–3.10 (m, 1H), 2.88–2.82 (m, 1H), 2.27–2.19 (m, 1H), 2.13–2.05 (m, 1H), 2.01–1.95 (m, 1H), 1.91–1.82 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$, ppm): δ 196.53, 170.32, 153.00, 138.64, 134.46, 129.62, 127.45, 125.56, 124.97, 122.92, 122.57, 118.91, 113.38, 104.28, 32.22, 31.90, 19.92; **IR** (KBr, cm^{-1}): 2926, 2853, 1920, 1737, 1620, 1460, 1227, 1165, 754; **HRMS** (ESI): Calcd For $C_{17}H_{15}O_3^+$ $[M + H]^+$: 267.1016, found 267.1009.

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