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Oxidative Catalytic Spiroketalization Leading to Diastereoselective Synthesis of Spiro[benzofuran-2,1'-isochromene]s

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Abstract. A new one-pot, two-step silver-catalyzed spiroketalization of the *in-situ* generated quinone imine ketals (QIKs) with β-alkynyl ketones has been established, enabling multiple C−O and C−C bond-forming reactions to access densely functionalized spiro[benzofuran-2,1'-isochromene] derivatives with generally good yields. The use of *β*-alkynyl ketones bearing alkyl and aryl groups located at the α-position of the carbonyl group could lead to highly diastereoselective spiro[chromane-2,1'-isochromene] derivatives. The reaction features broad substrate scope, mild oxidative catalytic conditions and excellent diastereoselectivity.

Keywords: Spiroketalization; 1,4-Addition; Silver Catalysis; Benzannulated 5,6-Spiroketals; Diastereoselectivity

Introduction

Spiroketal is a privileged structural unit that exists widely in a range of natural products that exhibit interesting biological activity.[1] Among the family of spiroketals, benzannulated 5,6-spiroketals behave as a key pharmacophore in many bioactive natural products, such as *β*-rubromycin,[2] heliquinomycin,[3] griseorhodin A[4] (Figure 1). General strategies to access this key motif are through oxidative spiroketalization,[5] gold-catalyzed intramolecular alkyne hydroalkoxylation,[6] Pd-catalyzed reductive coupling,[7] copper(I)-catalyzed spiroketalization of propargyl alcohols,[8] Sc(OTf)$_3$-catalyzd epoxide-opening spiroketalizations,[9] multi-step spiroketalization of aryl acetylenes[10] or ketones,[11] hetero-Diels-Alder reaction of *o*-quinone methide precursors.[12] Very recently, Xu and co-workers reported a gold/Lewis acid co-catalyzed bicyclization of *o*-alkynyl benzyl alcohols toward benzannulated 5,6-spiroketals (Schemes 1a and 1b).[13] Despite these advances, the development of a general and practical protocol toward new functionalized benzannulated 5,6-spiroketals, starting from readily available substrates under mild conditions, is still highly desirable.

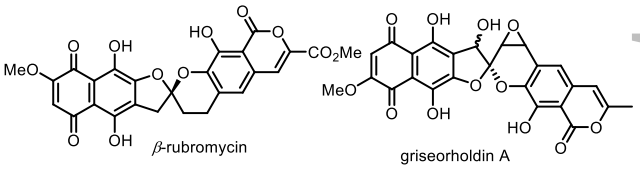

Figure 1. Spirocyclic natural products

On the other hand, catalytic cyclization of *β*-alkynyl ketones has proven to be a powerful tool for the collection of biologically interesting cyclic structures in a convergent manner.[14] Since the group of Yamamoto pioneered AuCl$_3$-catalyzed benzannulation of *β*-alkynyl ketones with alkynes,[15] catalytic cyclization cascades of *β*-alkynyl ketones have been investigated extensively.[16] Recently, we have developed a Ag/Brønsted acid co-catalyzed bicyclization reaction of *β*-alkynyl ketones with *para*-quinone methides (*p*-QMs), which provided a series of functionalized benzannulated 6,6-spiroketals.[17] During this project, we reasoned that catalytic conversion of *β*-alkynyl ketones into electron-rich methyleneisochromenes enables 1.4-addition and

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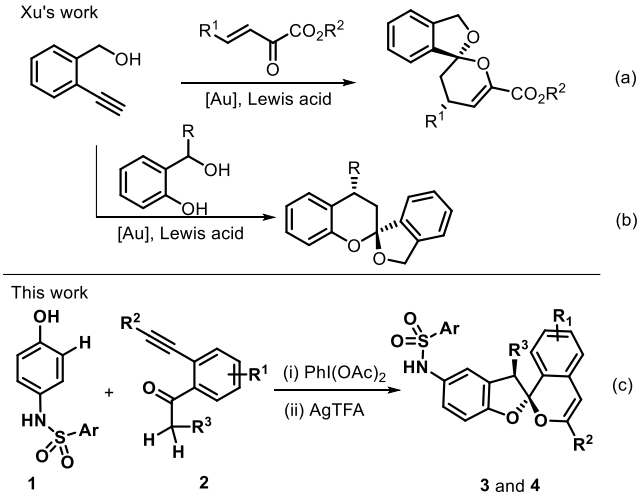
nucleophilic cyclization with quinone imine ketals (QIKs), generated *in situ* from *N*-(4-hydroxyphenyl) sulfonamides,[18] to access new functionalized benzannulated 5,6-spiroketals. As anticipated, *N*-(4-hydroxyphenyl) sulfonamides could be oxidized by phenyliodine diacetate (PIDA) to QIKs, followed by the interception of methyleneisochromenes from *β*-alkynyl ketones through silver catalysis, giving access to the desired spiro[benzofuran-2,1'-isochromene] derivatives with excellent diastereoselectivity in an atom-economic fashion. (Scheme 1c). Notably, the one-pot, two-step spiroketalization reaction occurred smoothly to give the desired products, avoiding the pre-preparation of QIKs, which demanded a complicated process for their preparation.[18] The current protocol represents a new and reliable silver catalysis for forming diastereoselective benzannulated 5,6-spiroketals with a sulfonamide functionality together with C(sp^3)-H functionalization of *β*-alkynyl ketones and C(sp^2)-H functionalization of *N*-(4-hydroxyphenyl) sulfonamides in a one-pot fashion. To the best of our knowledge, this oxidative silver catalysis toward benzannulated 5,6-spiroketals has been virtually unexplored. Herein, we report this attractive and useful transformation.

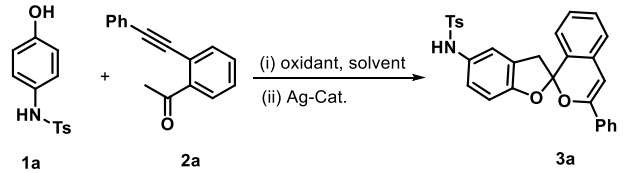
Scheme 1. Profiles of metal-catalyzed spiroketalization



Results and Discussion

We began our investigations by selecting *N*-(4-hydroxyphenyl) sulfonamide **1a** and *β*-alkynyl ketone **2a** as model substrates. At the beginning, *N*-(4-hydroxyphenyl) sulfonamide **1a** was subjected with 2.0 equivalents of PIDA ($PhI(OAc)_2$) in toluene at room temperature for 5 hours. Without isolation, *β*-alkynyl ketone **2a** and AgOTf (10 mol %) were then added into the above reaction system. The reaction proceeded to access the desired product **3a**, albeit with a low 21% yield (Table 1, entry 1). Exchanging AgOTf for $AgNO_3$ resulted in a higher yield (47%, entry 2). To our delight, the use of silver trifluoroacetate as catalyst could significantly facilitate this transformation and provided **3a** in 82% yield (entry 3). In contrast, AgOAc and AgF completely suppressed the reaction

Table 1 Optimization of the reaction conditions[a]



1a 2a 3a

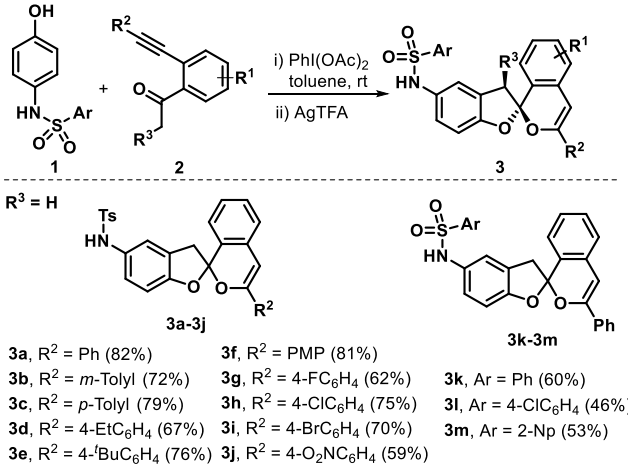
entry	Oxidant (equiv)	Cat. (mol %)	solvent	Yield (%)[b]
1	PIDA (2.0)	AgOTf (10)	toluene	21
2	PIDA (2.0)	$AgNO_3$ (10)	toluene	47
3	PIDA (2.0)	CF_3CO_2Ag (10)	toluene	82
4	PIDA (2.0)	AgOAc (10)	toluene	ND
5	PIDA (2.0)	AgF (10)	toluene	trace
6	$Na_2Cr_2O_7$ (2.0)	CF_3CO_2Ag (10)	toluene	ND
7	$K_2S_2O_8$ (2.0)	CF_3CO_2Ag (10)	toluene	trace
8	Oxone (2.0)	CF_3CO_2Ag (10)	toluene	trace
9	TBHP(2.0)	CF_3CO_2Ag (10)	toluene	trace
10	mCPBA (2.0)	CF_3CO_2Ag (10)	toluene	trace
11	IBX (2.0)	CF_3CO_2Ag (10)	toluene	74
12	PIFA (2.0)	CF_3CO_2Ag (10)	toluene	80
13	PIDA (2.0)	CF_3CO_2Ag (10)	1,4-dioxane	12[c]
14	PIDA (2.0)	CF_3CO_2Ag (10)	DCM	77
15	PIDA (2.0)	CF_3CO_2Ag (10)	$CHCl_3$	65
16	PIDA (2.0)	CF_3CO_2Ag (10)	DCE	56
17	PIDA (2.0)	CF_3CO_2Ag (10)	DMF	trace
18	PIDA (2.0)	CF_3CO_2Ag (10)	EtOH	trace
19	PIDA (2.0)	CF_3CO_2Ag (10)	CH_3CN	76
20	PIDA (2.0)	CF_3CO_2Ag (10)	toluene	71[c]
21	PIDA (2.0)	CF_3CO_2Ag (10)	toluene	64[d]

[a]Reaction conditions: (i) **1a** (0.5 mmol), oxidant (1.0 mmol) and toluene (2 mL) in the seal reaction tube under air conditions at room temperature for 5 hours. (ii) **2a** (0.2 mmol) in 1.0 mL of toluene was added by syringe pump in 0.5 hour. Then, the reaction system was stirred at room temperature for 7 hours.
[b]Isolated yield is based on **2a**.
[c]The reaction was carried out at 20 °C.
[d]The reaction was carried out at 40 °C

process (entries 4-5). Encouraged by these outcomes, we considered to exploit different oxidants and solvents to search for the optimal reaction conditions. The screening of several other inorganic and organic oxidants (2.0 equiv.) revealed that, compared with $Na_2Cr_2O_7$, $K_2S_2O_8$, oxone, *tert*-butyl hydroperoxide (TBHP, 70% in water), *m*-chloroperoxybenzoic acid

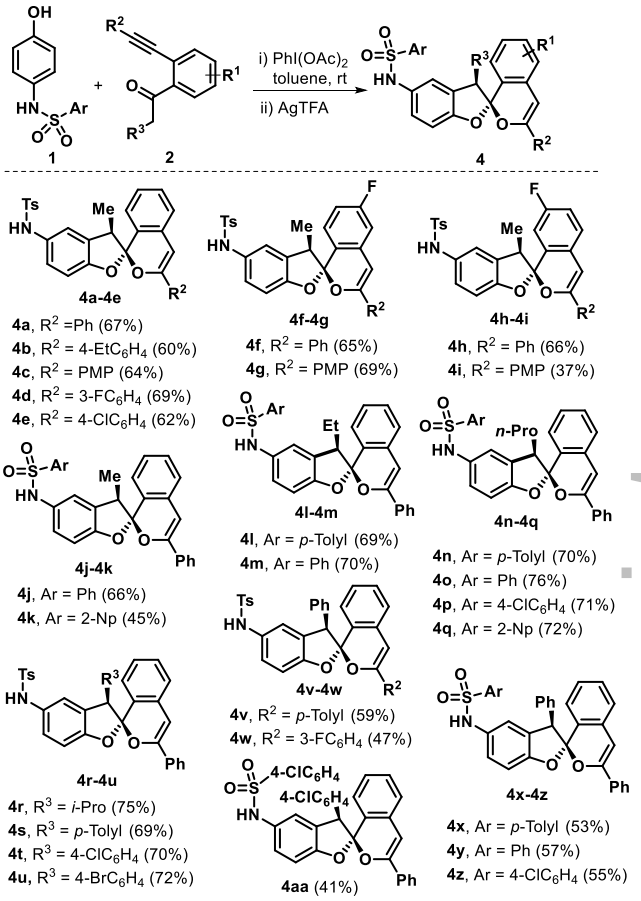
(mCPBA), 2-iodoxybenzoic acid (IBX), and phenyliodine bis(trifluoroacetate) (PIFA) (entries 6−12), phenyliodine diacetate (PIDA) still gave the best result in this spiroketalization (entry 3). Next, the solvent effect of this transformation was investigated. As shown in Table 1, toluene was proved to be an effective medium for this silver catalysis (entry 3). The other solvents, such as 1,4-dioxane, dichloromethane (DCM), trichloromethane ($CHCl_3$), 1,2-dichloroethane (DCE), *N*,*N*-dimethylformamide (DMF), ethanol (EtOH), and acetonitrile (CH_3CN), all gave unsatisfactory outcomes (entries 13-19). Lower conversion of **3a** was observed with the reaction temperature being at either 20 °C or 40 °C (entries 20-21).

Scheme 2. Substrate scope for synthesis of **3**.



3a, R^2 = Ph (82%)
3b, R^2 = *m*-Tolyl (72%)
3c, R^2 = *p*-Tolyl (79%)
3d, R^2 = 4-EtC_6H_4 (67%)
3e, R^2 = 4-^{t}BuC_6H_4 (76%)
3f, R^2 = PMP (81%)
3g, R^2 = 4-FC_6H_4 (62%)
3h, R^2 = 4-ClC_6H_4 (75%)
3i, R^2 = 4-BrC_6H_4 (70%)
3j, R^2 = 4-O_2NC_6H_4 (59%)
3k, Ar = Ph (60%)
3l, Ar = 4-ClC_6H_4 (46%)
3m, Ar = 2-Np (53%)

Scheme 3. Substrate scope for synthesis of **4**.



4a, R^2 =Ph (67%)
4b, R^2 = 4-EtC_6H_4 (60%)
4c, R^2 = PMP (64%)
4d, R^2 = 3-FC_6H_4 (69%)
4e, R^2 = 4-ClC_6H_4 (62%)
4f, R^2 = Ph (65%)
4g, R^2 = PMP (69%)
4h, R^2 = Ph (66%)
4i, R^2 = PMP (37%)
4j, Ar = Ph (66%)
4k, Ar = 2-Np (45%)
4l, Ar = *p*-Tolyl (69%)
4m, Ar = Ph (70%)
4n, Ar = *p*-Tolyl (70%)
4o, Ar = Ph (76%)
4p, Ar = 4-ClC_6H_4 (71%)
4q, Ar = 2-Np (72%)
4r, R^3 = *i*-Pro (75%)
4s, R^3 = *p*-Tolyl (69%)
4t, R^3 = 4-ClC_6H_4 (70%)
4u, R^3 = 4-BrC_6H_4 (72%)
4v, R^2 = *p*-Tolyl (59%)
4w, R^2 = 3-FC_6H_4 (47%)
4x, Ar = *p*-Tolyl (53%)
4y, Ar = Ph (57%)
4z, Ar = 4-ClC_6H_4 (55%)

With the acceptable reaction conditions for this silver catalysis in hand, we then set out to explore the scope of these transformations by examining *β*-alkynyl ketone and *N*-(4-hydroxyphenyl) sulfonamide components. At first, *β*-alkynyl ketones with diverse functionalities attached by arylalkynyl moiety (R^2) were explored in combination with *N*-(4-hydroxyphenyl) sulfonamide **1a**. Various substituents with electronically rich and deficient property did not hamper this Ag-catalyzed bicyclization process, delivering the corresponding dibenzannulated 5,6-spiroketals **3b**−**3j** with 59%-81% yields. Functional groups such as methyl (**2b** and **2c**), ethyl (**2d**), *t*-butyl (**2e**), methoxy (*p*-methoxyphenyl = PMP, **2f**), fluoro (**2g**), chloro (**2h**), bromo (**2i**), nitro (**2j**) were tolerated well under the standard conditions. The scope of *N*-(4-hydroxyphenyl)sulfonamides was then investigated by utilizing *β*-alkynyl ketone **2a** as a representative reaction partner. As expected, the variant of aryl groups directly bound to sulfonamide unit such as phenyl (**1b**), 4-chlorophenyl (**1c**) and naphthalen-2-yl (2-Np, **1d**) all worked readily with these oxidative catalytic conditions, affording the corresponding products **3k-3m** in 46%-60% yields. Next, we decided to change the substituents located at *α*-position of the carbonyl group on the *β*-alkynyl ketone unit to expand its synthetic utility. As shown in Scheme 3, a large variety of different substituents including alkyl (methyl, ethyl, *n*-propyl, and *i*-propyl) and aryl groups would be accommodated, confirming the success of the reaction, as the corresponding products **4a**–**4aa** as sole diastereoisomers were generated in 37%–76% yields. Among which, substrates **2** carrying the fluoro

functionality at 4- or 5-position of the internal arene ring were successfully engaged in the silver catalysis, enabling 6-*endo-dig* cyclization/1,4-addition-cyclization cascades to access diastereoenriched dibenzannulated 5,6-spiroketals **4f-4i** in 37%-69% yields. It is noteworthy that the present protocol represents a reliable new and practical pathway for flexible synthesis of a series of richly functionalized dibenzannulated 5,6-spiroketals **4** with generally excellent diastereoselectvity through Ag-catalyzed bicyclization involving C(sp^3)−H functionalization of *β*-alkynyl ketones. The structures of these spiroketals **3** were fully characterized by their NMR spectroscopy and HRMS. In the case of **4x**, its stereoscopic structure was unequivocally determined by conducting single crystal X-ray diffraction (Figure 2).[19]

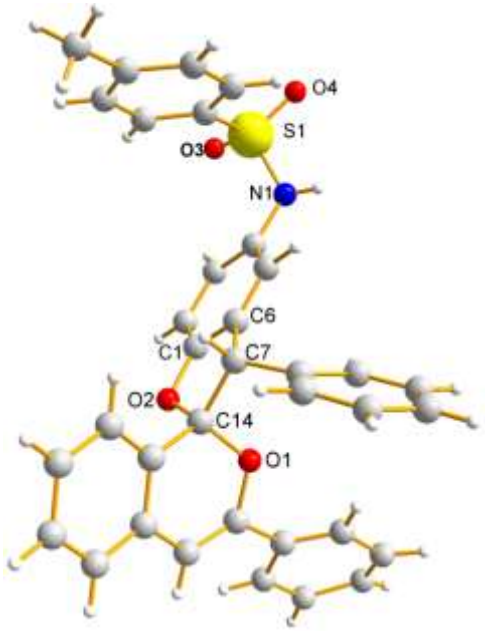
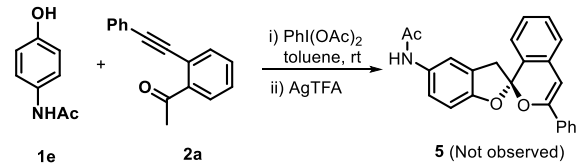
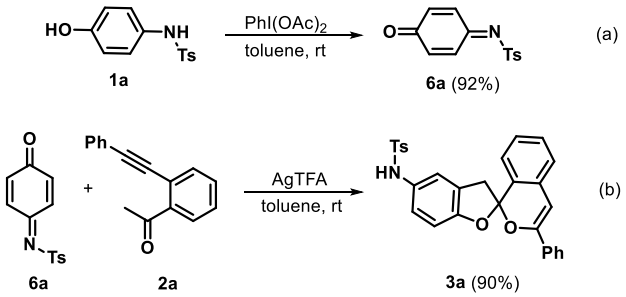


Figure 2. ORTEP drawing of **4x**

To expand potential application of this method, the two-step reaction of *N*-acetyl protected 4-aminophenol **1e** with *β*-alkynyl ketone **2a** was conducted under the standard conditions. Regrettably, the reaction did not give the desired product **5** as the starting material **1e** was recovered (Scheme 4).

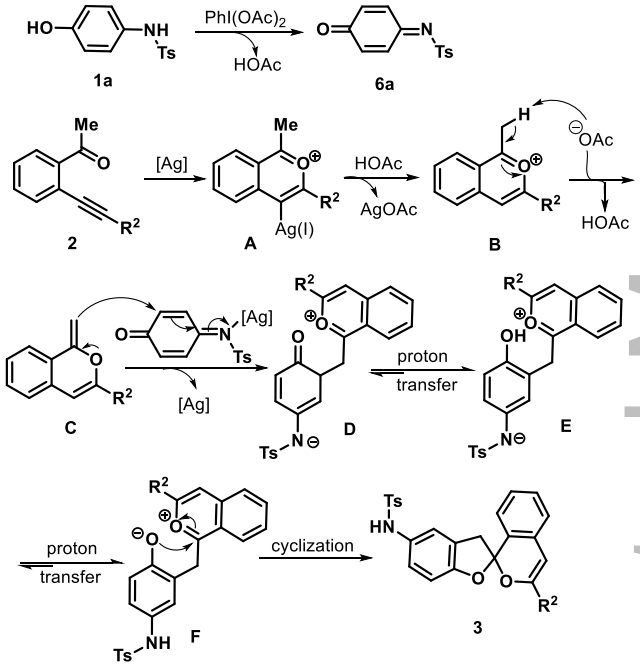


Scheme 4. Two-step reaction of *N*-acetyl-protected **1e**



Scheme 5. Control experiments

To understand the mechanism, *N*-(4-hydroxyphenyl)sulfonamide **1a** was first oxidized by phenyliodine diacetate (PIDA) to give QIK **6a** in 92% yield (Scheme 5a). Then, the preformed QIK **6a** was subjected with the reaction of *β*-alkynyl ketone **2a** in the presence of CF_3CO_2Ag, providing the corresponding product **3a** in 90% yield (Scheme 5b), indicating that QIK could act as an intermediate for the synthesis of **3** and **4**.



Scheme 6. Proposed reaction mechanism

Based on the above observations and previous literature survey,[14-16] we propose a tentative pathway for this transformation as described in Scheme 6. Initially, *N*-(4-hydroxyphenyl) sulfonamide **1a** was oxidized by phenyliodine diacetate (PIDA) to yield QIK **6a** and HOAc. Next, Ag-catalyzed 6-*endo-dig* oxo-cyclization of *β*-alkynyl ketones **2**[20] in the presence of HOAc generates intermediate **C** through continuous proton transfer (**A** to **C**). Ag-catalyzed 1,4-conjugate addition of intermediate **C** into QIK **6a** gives adduct **D**, followed by twice proton transfer to intermediate **F**, which undergoes oxo-nucleophilic addition (oxo-cyclization) to generate final products **3**.

Conclusion

In summary, starting from *N*-(4-hydroxyphenyl)sulfonamides and *β*-alkynyl ketones, we have established one-pot, two-step Ag-catalyzed spiroketalization cascades involving PIDA-mediated in situ formation of QIKs, Ag-catalyzed 6-*endo*-*dig* oxo-cyclization and 1,4-conjugate addition as well as oxo-nucleophilic addition, in which a wide range of structurally diverse spiro[benzofuran-2,1'-isochromene] derivatives with generally good yields were synthesized. *β*-Alkynyl ketones bearing alkyl and aryl groups located at α-position of the carbonyl group could participate in this oxidative silver catalysis, leading to highly diastereoselective spiro[chromane-2,1'-isochromene] derivatives with generally good yields. The present oxidative catalytic system provides a general and practical pathway for constructing dibenzannulated 5,6-spiroketals together with C(sp^3)-H functionalization of *β*-alkynyl ketones and C(sp^2)-H functionalization of *N*-(4-hydroxyphenyl) sulfonamides in a one-pot fashion. Further investigation of the bioactivity of these spiroketals is underway.

Experimental Section

Typical Procedure for the Preparation of 3a:

N-(4-Hydroxyphenyl)-4-methylbenzenesulfonamide (**1a**, 0.5 mmol, 131 g), iodobenzene diacetate (2.0 equiv, 322 mg) and toluene (2.0 mL) were added into a 10-mL Schlenk tube. The mixture was stirred at room temperature for about 5 hours. After the reaction was complete, 10 mol% of silver trifluoroacetate was added and the system was cooled to 0 °C. Then, 1-(2-(phenylethynyl)phenyl) ethan-1-one (**2a**, 0.2 mmol, 44 mg) was dissolved in 1.0 mL of toluene and added to the above reaction system by syringe pump in 0.5 hour. Then, the reaction system was stirred at room temperature for about 7 hours under the starting material **2a** completely disappeared as monitored by TLC. The solution was then extracted with EtOAc, the combined organic layers were dried over anhydrous Na_2SO_4, filtered, and evaporated under vacuum. The residue was purified by column chromatography on silica gel to afford the desired product **3a**.

4-methyl-*N*-(3'-phenyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)benzenesulfonamide (3a)
White solid, 79.0 mg, 82% yield; mp: 176-177 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72-7.68 (m, 4H), 7.49-7.29 (m, 9H), 6.77 (d, *J* = 8.0 Hz, 1H), 6.70-6.68, 6.64-6.62 (m, 1H), 4.11 (d, *J* = 17.3 Hz, 1H), 3.74 (d, *J* = 17.2 Hz, 1H), 2.45(s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.6, 149.7, 143.9, 136.2, 134.0, 130.9, 130.0, 129.7, 129.1, 128.5, 127.5, 127.3, 127.2, 126.7, 125.2(3), 125.2(0), 124.8, 124.4, 121.6, 111.5, 110.2, 101.0, 41.3, 21.7. HRMS (ESI) *m/z*: calcd for $[C_{29}H_{23}NO_4S+Na]^+$ requires: 504.1245 $[M+Na]^+$; found: 504.1240.

4-methyl-*N*-(3'-(*m*-tolyl)-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)benzenesulfonamide (3b)
White solid, 71.1 mg, 72% yield; mp: 209-210 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65-7.62 (m, 2H), 7.46-7.36 (m, 4H), 7.31-7.29 (m, 2H), 7.27-7.24 (m, 2H), 7.22-7.20 (m, 1H), 7.14 (d, *J* = 7.5 Hz, 1H), 6.71-6.68 (m, 1H), 6.64 (s, 1H), 6.58 (d, *J* = 8.4 Hz, 1H), 6.37 (s, 1H), 4.07 (d, *J* = 17.3 Hz, 1H), 3.71 (d, *J* = 17.3 Hz, 1H), 2.41 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7, 149.8, 143.8, 138.1, 136.2, 134.0, 130.9, 129.9, 129.7, 129.6, 128.4, 127.5, 127.2, 126.7, 125.8, 125.2, 125.0, 124.3, 122.4, 121.8, 111.5, 110.2, 100.9, 41.4, 21.7, 21.6. HRMS (ESI) *m/z*: calcd for $[C_{29}H_{23}NO_4SNa]^+$ requires: 518.1402 $[M+Na]^+$; found: 518.1398.

4-methyl-*N*-(3'-(*p*-tolyl)-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)benzenesulfonamide (3c)
White solid, 78.2 mg, 79% yield; mp: 199-200 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65-7.63 (m, 2H), 7.54-7.52 (m, 2H), 7.44-7.36 (m, 2H), 7.31-7.26 (m, 3H), 7.20 (d, *J* = 1.6 Hz, 1H), 7.15 (d, *J* = 8.1 Hz, 2H), 6.71-6.69 (m, 1H), 6.61 (s, 1H), 6.57 (d, *J* = 8.4 Hz, 1H), 6.42 (s, 1H), 4.07 (d, *J* = 17.2 Hz, 1H), 3.69 (d, *J* = 17.2 Hz, 1H), 2.41 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7, 149.8, 143.8, 139.2, 136.2, 131.2, 131.0, 129.9, 129.7, 129.6, 129.2, 127.5, 127.1, 127.0, 126.7, 125.2, 125.1, 124.3, 121.7, 111.5, 110.2, 100.3, 41.3, 21.7, 21.4. HRMS (ESI) *m/z*: calcd for$[C_{30}H_{25}NO_4SNa]^+$ requires: 518.1402 $[M+Na]^+$; found: 518.1396.

***N*-(3'-(4-ethylphenyl)-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)-4-methylbenzenesulfonamide (3d)**
White solid, 68.3 mg, 67% yield; mp: 198-199 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66-7.62 (m, 2H), 7.58-7.54 (m, 2H), 7.43-7.37 (m, 2H), 7.30 (s, 1H), 7.28-7.26 (m, 3H), 7.21 (d, *J* = 2.0 Hz, 1H), 7.19-7.17 (m, 2H), 6.71-6.69 (m, 1H), 6.62 (s, 1H), 6.57 (d, *J* = 8.4 Hz, 1H), 6.43 (s, 1H), 4.07 (d, *J* = 17.2 Hz, 1H), 3.69 (d, *J* = 17.3 Hz, 1H), 2.65 (q, *J* = 7.6 Hz, 2H), 2.41 (s, 3H), 1.23 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7, 149.8, 145.6, 143.8, 136.1, 131.5, 131.1, 129.9, 129.7, 129.5, 128.0, 127.5, 127.0, 126.7, 125.2, 125.1, 124.9, 124.3, 121.7, 111.5, 110.2, 100.3, 41.3, 28.8, 21.7, 15.6. HRMS (ESI) *m/z*: calcd for $[C_{31}H_{27}NO_4SNa]^+$ requires: 532.1558 $[M+Na]^+$; found: 532.1553.

***N*-(3'-(4-(*tert*-butyl)phenyl)-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)-4-methylbenzenesulfonamide (3e)**
White solid, 81.8 mg, 76% yield; mp: 201-202 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.1 Hz, 2H), 7.58 (d, *J* = 8.4 Hz, 2H), 7.43-7.37 (m, 4H), 7.30-7.22 (m, 4H), 6.73 (dd, *J* = 8.3, 1.4 Hz, 1H), 6.66-6.62 (m, 2H), 6.57 (d, *J* = 8.4 Hz, 1H), 4.07 (d, *J* = 17.2 Hz, 1H), 3.68 (d, *J* = 17.2 Hz, 1H), 2.41 (s, 3H), 1.32 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.6, 152.4, 149.8, 143.8, 136.2, 131.18 (d, *J* = 15.7 Hz), 129.9, 129.67 (d, *J* = 5.0 Hz), 127.5, 127.03 (d, *J* = 3.7 Hz), 126.7, 125.4, 124.97 (t, *J* = 15.8 Hz), 124.4, 121.6, 111.5, 110.2, 100.4, 41.2, 34.8, 31.3, 21.7. HRMS (ESI) *m/z*: calcd for $[C_{33}H_{31}NO_4SH]^+$ requires: 538.2052 $[M+H]^+$; found: 538.2051.

***N*-(3'-(4-methoxyphenyl)-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)-4-methylbenzenesulfonamide (3f)**
White solid, 82.9 mg, 81% yield; mp: 186-187 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68-7.62 (m, 2H), 7.60-7.54 (m, 2H), 7.42-7.35 (m, 2H), 7.29-7.26 (m, 3H), 7.21 (d, *J* = 2.0 Hz, 1H), 6.91-6.83 (m, 2H), 6.71 (dd, *J* = 8.5, 2.3 Hz, 1H), 6.58 (d, *J* = 8.4 Hz, 1H), 6.54-6.52 (m, 2H), 4.06 (d, *J* = 17.2 Hz, 1H), 3.81 (s, 3H), 3.68 (d, *J* = 17.3 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 155.6, 149.6, 143.9, 136.2, 131.2, 129.9, 129.7, 129.6, 127.5, 126.9, 126.8, 126.7, 126.6, 125.0, 124.9, 124.3, 121.7, 113.9, 111.5, 110.2, 99.4,

55.4, 41.2, 21.7. HRMS (ESI) *m/z*: calcd for $[C_{30}H_{25}NO_5SNa]^+$ requires: 534.1351 $[M+Na]^+$; found: 534.1346.

***N*-(3'-(4-fluorophenyl)-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)-4-methylbenzenesulfonamide (3g)**

White solid, 61.9 mg, 62% yield; mp: 176-177 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66-7.58 (m, 4H), 7.44-7.37 (m, 2H), 7.33-7.27 (m, 3H), 7.22 (d, *J* = 2.0 Hz, 1H), 7.07-6.99 (m, 2H), 6.70 (dd, *J* = 8.4, 2.3 Hz, 1H), 6.58 (t, *J* = 4.2 Hz, 2H), 6.40 (s, 1H), 4.08 (d, *J* = 17.3 Hz, 1H), 3.69 (d, *J* = 17.3 Hz, 1H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.6, 148.8, 143.9, 136.2, 130.7, 130.2 (d, *J* = 3.1 Hz), 130.0, 129.7, 127.5, 127.2 (d, *J* = 16.0 Hz), 127.4 (d, *J* = 4.0 Hz), 126.6, 125.2, 124.9, 124.4, 121.7, 115.6, 115.4, 111.5, 110.2, 100.8 (d, *J* = 1.7 Hz), 41.3, 21.7. HRMS (ESI) *m/z*: calcd for $[C_{29}H_{23}FNO_4S]^+$ requires: 500.1332 $[M+H]^+$; found: 500.1344.

***N*-(3'-(4-chlorophenyl)-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)-4-methylbenzenesulfonamide (3h)**

White solid, 77.5 mg, 75% yield; mp: 190-191 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.0 Hz, 2H), 7.56 (d, *J* = 8.3 Hz, 2H), 7.45-7.37 (m, 2H), 7.34-7.27 (m, 5H), 7.23 (s, 1H), 6.70 (d, *J* = 8.0 Hz, 1H), 6.64 (s, 1H), 6.58 (d, *J* = 8.5 Hz, 1H), 6.41 (s, 1H), 4.08 (d, *J* = 17.2 Hz, 1H), 3.69 (d, *J* = 17.3 Hz, 1H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.5, 148.6, 143.9, 136.2, 134.9, 132.5, 130.6, 130.0, 129.7(1), 129.7(0) 128.7, 127.5, 127.4, 127.2, 126.6, 126.4, 125.3, 124.9, 124.4, 121.7, 111.5, 110.2, 101.4, 41.3, 21.7. HRMS (ESI) *m/z*: calcd for $[C_{29}H_{22}ClNO_4SNa]^+$ requires: 538.0856 $[M+Na]^+$; found: 538.0850.

***N*-(3'-(4-bromophenyl)-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)-4-methylbenzenesulfonamide (3i)**

White solid, 78.2 mg, 70% yield; mp: 207-208 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.92 (s, 1H), 7.61-7.59 (m, 2H), 7.56-7.48 (m, 5H), 7.45-7.41 (m, 1H), 7.36-7.27 (m, 4H), 7.14-7.00 (m, 2H), 6.77 (dd, *J* = 8.5, 1.6 Hz, 1H), 6.55 (d, *J* = 8.5 Hz, 1H), 4.20 (d, *J* = 17.6 Hz, 1H), 3.57 (d, *J* = 17.6 Hz, 1H), 2.31 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 153.9, 147.9, 143.5, 137.3, 133.2, 132.1, 131.8, 130.8, 130.5, 130.1, 128.0, 127.3, 127.1, 127.0, 125.7, 125.3, 122.8, 122.4, 119.5, 111.4, 110.0, 102.4, 21.5. HRMS (ESI) *m/z*: calcd for $[C_{29}H_{23}BrNO_4S]^+$ requires: 560.0531 $[M+H]^+$; found: 560.0532.

4-methyl-*N*-(3'-(4-nitrophenyl)-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)benzenesulfonamide (3j)

White solid, 62.0 mg, 59% yield; mp: 187-188 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.95 (s, 1H), 7.70-7.53 (m, 5H), 7.48 (m, 1H), 7.43-7.28 (m, 7H), 7.19-6.98 (m, 2H), 6.82 (dd, *J* = 8.5, 2.0 Hz, 1H), 6.61 (d, *J* = 8.5 Hz, 1H), 4.25 (d, *J* = 17.5 Hz, 1H), 3.62 (d, *J* = 17.6 Hz, 1H), 2.36 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 154.0, 148.9, 143.5, 137.2, 133.9, 131.7, 131.0, 130.3, 130.0, 129.6, 129.0, 127.7, 127.2, 127.1(6), 127.1(4), 125.5, 125.2, 125.0, 122.4, 119.6, 111.3, 109.9, 101.6, 21.5. HRMS (ESI) *m/z*: calcd for $[C_{29}H_{22}N_2O_6SNa]^+$ requires: 549.1096 $[M+Na]^+$; found: 549.1099.

***N*-(3'-phenyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)benzenesulfonamide (3k)**

White solid, 56.1 mg, 60% yield; mp: 199-200 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78-7.75 (m, 2H), 7.67-7.60 (m, 2H), 7.59-7.56 (m, 1H), 7.50-7.46 (m, 2H), 7.44-7.20 (m, 8H), 6.73 (dd, *J* = 8.4, 1.7 Hz, 1H), 6.66 (s, 1H), 6.58 (d, *J* = 8.5 Hz, 2H), 4.07 (d, *J* = 17.3 Hz, 1H), 3.69 (d, *J* = 17.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0, 149.6, 138.8, 135.0, 133.9, 133.0, 131.7, 130.3, 130.0, 129.7, 129.1, 128.9, 128.3, 128.2, 127.8, 127.5, 127.1, 126.1, 125.9, 125.4, 124.9, 124.7, 122.0, 112.6, 110.8, 100.3, 56.6. HRMS (ESI) *m/z*: calcd for $[C_{28}H_{22}NO_4S]^+$ requires: 468.1270 $[M+H]^+$; found: 468.1272.

4-chloro-*N*-(3'-phenyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)benzenesulfonamide (3l)

White solid, 46.3 mg, 46% yield; mp: 195-196 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72-7.67 (m, 2H), 7.65-7.62 (m, 2H), 7.46-7.43 (m, 3H), 7.40-7.29 (m, 6H), 7.20 (m, 1H), 6.74 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.66 (s, 1H), 6.61 (d, *J* = 8.4 Hz, 1H), 6.54 (s, 1H), 4.09 (d, *J* = 17.3 Hz, 1H), 3.71 (d, *J* = 17.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 149.69, 139.69, 137.6, 134.0, 130.9, 130.1, 129.4, 129.2, 129.1, 128.9, 128.5, 127.3, 127.0, 126.9, 125.3, 125.2, 125.1, 124.4, 121.8, 111.6, 110.4, 101.1, 41.3. HRMS (ESI) *m/z*: calcd for $[C_{28}H_{21}ClNO_4S]^+$ requires: 502.0880 $[M+H]^+$; found: 502.0877.

***N*-(3'-phenyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)naphthalene-2-sulfonamide (3m)**

White solid, 54.9 mg, 53% yield; mp: 181-182 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 1.2 Hz, 1H), 7.94-7.87 (m, 3H), 7.74 (m, 1H), 7.66-7.60 (m, 3H), 7.60-7.55 (m, 1H), 7.42-7.38 (m, 1H), 7.35-7.32 (m, 4H), 7.30-7.26 (m, 2H), 7.21-7.17 (m, 1H), 6.73 (dd, *J* = 8.5, 2.3 Hz, 1H), 6.63 (s, 1H), 6.54 (m, 2H), 4.03 (d, *J* = 17.2 Hz, 1H), 3.66 (d, *J* = 17.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.8, 149.7, 136.0, 135.0, 134.0, 132.2, 130.8, 129.9, 129.4(1), 129.4(0), 129.1, 129.0, 128.9, 128.5, 128.0, 127.7, 127.2, 127.1, 126.7, 125.2, 125.1, 124.4, 122.6, 121.8, 111.5, 110.3, 101.0, 41.3. HRMS (ESI) *m/z*: calcd for $[C_{32}H_{24}NO_4S]^+$ requires: 518.1426 $[M+H]^+$; found: 518.1436.

4-methyl-*N*-(3-methyl-3'-phenyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)benzenesulfonamide (4a)

White solid, 66.5 mg, 67% yield; mp: 182-183 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.68 (m, 1H), 7.64-7.62 (m, 2H), 7.46-7.43 (m, 1H), 7.39-7.36 (m, 3H), 7.30-7.27 (m, 4H), 7.25 (d, *J* = 1.1 Hz, 1H), 7.22-7.18 (m, 5H), 6.98 (dd, *J* = 8.4, 1.7 Hz, 1H), 6.91-6.89 (m, 1H), 6.74 (d, *J* = 8.4 Hz, 1H), 6.54 (s, 1H), 6.43 (s, 1H), 5.45 (s, 1H), 4.14 (q, *J* = 7.1 Hz, 1H), 2.43 (s, 3H), 1.44-1.10 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 149.6, 143.8, 136.0, 135.1, 133.9, 131.7, 130.1, 130.0, 129.9, 129.7, 128.8, 128.3, 128.2, 127.8, 127.6, 127.1, 126.3, 125.8, 125.3, 124.9, 124.6, 122.0, 112.6, 110.7, 100.2, 60.5, 56.8, 21.7, 21.2, 14.3. HRMS (ESI) *m/z*: calcd for $[C_{30}H_{25}NO_4SNa]^+$ requires: 518.1402 $[M+Na]^+$; found: 518.1414.

***N*-(3'-(4-ethylphenyl)-3-methyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)-4-methylbenzenesulfonamide (4b)**

White solid, 62.9 mg, 60% yield; mp: 195-196 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.1 Hz, 2H), 7.51-7.39 (m, 4H), 7.32-7.27 (m, 2H), 7.27-7.24 (m, 1H), 7.16 (d, *J* = 8.1 Hz, 2H), 7.08 (s, 1H), 6.71-6.69 (m, 1H), 6.64-6.52 (m, 2H), 6.35 (s, 1H), 4.25 (q, *J* = 6.9 Hz, 1H), 2.65 (q, *J* = 7.6 Hz, 2H), 2.40 (s, 3H), 1.45 (d, *J* = 7.0 Hz, 3H), 1.22 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 149.8, 145.5, 143.8, 136.0, 132.6, 132.0, 131.6, 130.0, 129.7, 129.6, 128.0, 127.5, 126.9, 125.8, 125.2, 125.1, 124.4, 120.8, 112.8, 110.3, 99.8, 44.3, 28.8, 21.7, 15.6, 12.1.HRMS (ESI) *m/z*: calcd for

$[C_{32}H_{30}NO_4S]^+$ requires: 524.1896 $[M+H]^+$; found: 524.1895.

***N*-(3'-(4-methoxyphenyl)-3-methyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)-4-methylbenzenesulfonamide (4c)**

White solid, 67.3 mg, 64% yield; mp: 182-183 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.89 (s, 1H), 7.72 (d, *J* = 8.2 Hz, 1H), 7.68-7.60 (m, 3H), 7.48-7.44 (m, 3H), 7.38-7.25 (m, 3H), 7.33-7.22 (m, 2H), 7.06 (s, 1H), 6.94-6.92 (m, 2H), 6.81-6.79 (m, 2H), 6.60 (d, *J* = 8.4 Hz, 1H), 4.43 (q, *J* = 6.7 Hz, 1H), 3.77 (s, 3H), 2.36 (s, 3H), 1.33 (d, *J* = 6.9 Hz, 3H).^{13}C NMR (100 MHz, DMSO-d_6) δ 160.5, 153.4, 148.9, 143.5, 137.1, 132.6, 132.2, 131.7, 130.3, 130.0, 129.8, 127.3, 127.1, 126.5, 126.4, 126.1, 125.6, 125.2, 126.5 122.8, 118.7, 114.5, 112.6, 111.0, 99.4, 55.7, 21.5, 12.2. HRMS (ESI) m/z: calcd for $[C_{31}H_{27}NO_5SNa]^+$ requires: 548.1508 $[M+Na]^+$; found: 548.1519.

***N*-(3'-(3-fluorophenyl)-3-methyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)-4-methylbenzenesulfonamide (4d)**

White solid,70.9 mg, 69% yield; mp: 141-142 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.2 Hz, 2H), 7.47 (d, *J* = 8.5 Hz, 3H), 7.43 (d, *J* = 7.3 Hz, 1H), 7.34-7.30 (m, 3H), 7.26-7.24 (m, 2H), 7.11 (s, 1H), 6.71-6.67 (m, 1H), 6.61 (s, 1H), 6.57 (d, *J* = 8.3 Hz, 1H), 6.37 (s, 1H), 4.26 (q, *J* = 6.8 Hz, 1H), 2.41 (s, 3H), 1.46 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 161.8, 154.8, 148.3 (d, *J* = 2.9 Hz), 143.9, 136.4 (d, *J* = 8.1 Hz), 135.9, 132.3, 131.4, 130.1(d, *J* = 4.6 Hz), 129.6, 127.5, 126.1, 125.5, 125.0, 124.5, 120.6 (d, *J* = 4.7 Hz), 115.9, 115.7, 112.7, 112.1, 111.8, 110.3, 101.5, 44.5, 21.6, 12.0. HRMS (ESI) *m/z*: calcd for $[C_{30}H_{25}FNO_4S]^+$ requires: 514.1488 $[M+H]^+$; found: 514.1484.

***N*-(3'-(4-chlorophenyl)-3-methyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)-4-methylbenzenesulfonamide (4e)**

White solid, 65.5 mg, 62% yield; mp: 184-185 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63-7.61 (m, 2H), 7.49-7.46 (m, 3H), 7.43 (d, *J* = 7.3 Hz, 1H), 7.34-7.30 (m, 3H), 7.27-7.24 (m, 2H), 7.11 (s, 1H), 6.70 (d, *J* = 8.3 Hz, 1H), 6.61-6.56 (m, 1H), 6.57 (d, *J* = 8.3 Hz, 1H), 6.37 (s, 1H), 4.26 (q, *J* = 6.8 Hz, 1H), 2.41 (s, 3H), 1.46 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.9, 148.6, 143.9, 136.1, 134.9, 132.6, 132.4, 131.5, 130.1, 129.9, 129.6, 128.7, 127.5, 127.4, 126.3, 125.9, 125.4, 124.9, 124.5, 120.7, 112.8, 110.3, 100.9, 44.4, 21.7, 12.1. HRMS (ESI) *m/z*: calcd for $[C_{30}H_{24}ClNO_4SNa]^+$ requires: 552.1012 $[M+Na]^+$; found: 552.1006.

***N*-(6'-fluoro-3-methyl-3'-phenyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)-4-methylbenzenesulfonamide (4f)**

White solid, 66.5 mg, 65% yield; mp: 204-205 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64-7.53 (m, 4H), 7.33-7.30 (m, 3H), 7.18-6.98 (m, 4H), 6.73 (d, *J* = 7.5 Hz, 1H), 6.60-6.48 (m, 2H), 6.37 (s, 1H), 4.14 (d, *J* = 6.1 Hz, 1H), 2.40 (s, 3H), 1.46 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.3, 143.5, 137.0, 133.9, 132.5, 131.9, 130.0, 129.5, 129.1, 127.3, 124.7, 122.8, 118.6, 112.7, 112.4, 111.9 (d, *J* = 2.7 Hz), 110.1, 100.4, 43.3, 21.4, 12.0. HRMS (ESI) *m/z*: calcd for $[C_{30}H_{24}FNO_4SNa]^+$ requires: 536.1308 $[M+Na]^+$; found: 536.1298.

***N*-(6'-fluoro-3'-(4-methoxyphenyl)-3-methyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)-4-methylbenzenesulfonamide (4g)**

White solid, 75.0 mg, 69% yield; mp: 148-149 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.6-7.63 (m, 2H), 7.51-7.49 (m, 2H), 7.45-7.43 (m, 1H), 7.28-7.26 (m, 2H), 7.10 (s, 1H), 6.98-6.96 (m, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 6.73 (d, *J* = 7.6 Hz, 1H), 6.60 (d, *J* = 8.4 Hz, 1H), 6.45 (d, *J* = 15.3 Hz, 2H), 4.21 (q, *J* = 6.9 Hz, 1H), 3.83 (s, 3H), 1.46 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 154.8, 150.7, 143.8, 136.0, 132.2, 129.8, 129.5, 127.4, 126.7, 126.2, 125.0, 120.6, 113.9, 113.4, 112.6, 111.1, 110.2, 98.2, 65.9, 55.4, 44.6, 21.6, 12.0. HRMS (ESI) *m/z*: calcd for $[C_{31}H_{27}FNO_5S]^+$ requires: 544.1594 $[M+H]^+$; found: 544.1596.

***N*-(7'-fluoro-3-methyl-3'-phenyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)-4-methylbenzenesulfonamide (4h)**

White solid, 67.5 mg, 66% yield; mp: 230-231 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64-7.53 (m, 4H), 7.33-7.30 (m, 3H), 7.18-6.98 (m, 4H), 6.73 (d, *J* = 7.5 Hz, 1H), 6.60-6.58 (m, 2H), 6.37 (s, 1H), 4.14 (d, *J* = 6.1 Hz, 1H), 2.40 (s, 3H), 1.46 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.9, 162.4, 154.7, 150.7, 143.8, 136.0, 134.2 (d, *J* = 9.3 Hz), 133.6, 132.1, 129.9, 129.5 (d, *J* = 19.3 Hz), 128.5, 127.4, 126.6 (d, *J* = 9.1 Hz), 125.2 (d, *J* = 7.4 Hz), 124.9, 120.6, 113.9, 113.7, 112.5, 111.4, 111.2, 110.2, 99.8 (d, *J* = 2.4 Hz), 44.7, 21.6, 12.0.HRMS (ESI) *m/z*: calcd for $[C_{30}H_{24}FNO_4SNa]^+$ requires: 536.1308 $[M+Na]^+$; found: 536.1302.

***N*-(7'-fluoro-3'-(4-methoxyphenyl)-3-methyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)-4-methylbenzenesulfonamide (4i)**

White solid, 40.2 mg, 37% yield; mp: 181-182 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66-7.62 (m, 2H), 7.54-7.50 (m, 2H), 7.29-7.26 (m, 4H), 7.21-7.07 (m, 3H), 6.88 (d, *J* = 8.7 Hz, 3H), 6.77-6.75 (m, 1H), 6.62 (d, *J* = 8.4 Hz, 1H), 6.51 (s, 1H), 6.42-6.38 (m, 1H), 4.15 (q, *J* = 6.7 Hz, 1H), 3.83 (s, 4H), 2.43 (s, 4H), 1.48 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 154.8, 149.0 (d, *J* = 2.5 Hz), 143.9), 136.0, 132.2, 129.9, 129.6, 128.3 (d, *J* = 2.9 Hz), 127.5, 126.6 (dd, *J* = 16.9, 4.8 Hz), 125.2, 120.7, 117.3, 117.1, 113.9, 112.1 (d, *J* = 2.7 Hz), 111.7, 111.5, 110.3, 100.0, 98.1 (d, *J* = 1.1 Hz), 55.4, 44.7, 21.7, 12.2. HRMS (ESI) *m/z*: calcd for $[C_{31}H_{26}FNO_5SNa]^+$ requires: 566.1413 $[M+Na]^+$; found: 566.1409.

***N*-(3-methyl-3'-phenyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)benzenesulfonamide (4j)**

White solid, 63.6 mg, 66% yield; mp: 187-188 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76-7.65 (m, 2H), 7.61-7.53 (m, 2H), 7.51-7.40 (m, 4H), 7.38-7.28 (m, 5H), 7.09 (s, 1H), 6.76 (dd, *J* = 8.3, 1.7 Hz, 1H), 6.70 (s, 1H), 6.64 (s, 1H), 6.61 (d, *J* = 8.4 Hz, 1H), 4.27 (q, *J* = 7.0 Hz, 1H), 1.48 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 149.6, 139.6, 137.4, 134.1, 132.7, 131.8, 130.1, 129.3, 129.1, 128.9, 128.5, 127.1, 125.8, 125.4, 125.06 (d, *J* = 5.6 Hz), 124.44 (s), 120.7, 112.9, 110.4, 100.6, 44.4, 12.1. HRMS (ESI) *m/z*: calcd for $[C_{29}H_{243}NO_4S]^+$ requires: 482.1426 $[M+H]^+$; found: 482.1424.

***N*-(3-methyl-3'-phenyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)naphthalene-2-sulfonamide (4k)**

White solid, 47.8 mg, 45% yield; mp: 172-173 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 1.4 Hz, 1H), 7.93-7.88 (m,

3H), 7.75 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.64-7.58 (m, 1H), 7.59-7.54 (m, 3H), 7.44-7.40 (m, 2H), 7.32-7.27 (m, 5H), 7.10-7.08 (m, 1H), 6.77-6.74 (m, 1H), 6.65-6.62 (m, 2H), 6.55 (d, *J* = 8.4 Hz, 1H), 4.22 (q, *J* = 7.0 Hz, 1H), 1.40 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.0, 149.6, 135.9, 135.0, 134.1, 132.5, 132.1, 131.7, 130.0, 129.6, 129.4, 129.3, 129.0, 128.5, 128.0, 127.7, 127.1, 125.9, 125.1, 125.0, 124.4, 122.6, 120.7, 112.7, 110.3, 100.5, 44.4, 12.1. HRMS (ESI) *m/z*: calcd for $[C_{33}H_{26}NO_4S]^+$ requires: 532.1583 $[M+H]^+$; found: 532.1580.

***N*-(3-ethyl-3'-phenyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)-4-methylbenzenesulfonamide (4l)**

White solid, 70.1 mg, 69% yield; mp: 194-195 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64-7.62 (m, 2H), 7.60-7.56 (m, 2H), 7.49 (d, *J* = 7.9 Hz, 1H), 7.44-7.42 (m, 1H), 7.36-7.29 (m, 5H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.12 (s, 1H), 6.71 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.64 (s, 1H), 6.56 (d, *J* = 8.4 Hz, 1H), 4.14 (t, *J* = 7.3 Hz, 1H), 2.40 (s, 3H), 2.09-2.01 (m, 2H), 0.92 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.0, 149.4, 143.8, 136.0, 134.2, 131.8, 131.0, 129.9, 129.6, 129.0, 128.5, 127.5, 127.0, 125.4, 125.1, 125.0, 124.7, 121.0, 112.2, 110.2, 100.4, 50.5, 21.7, 21.5, 12.7.HRMS (ESI) *m/z*: calcd for $[C_{31}H_{28}NO_4S]^+$ requires: 510.1739 $[M+H]^+$; found: 510.1740.

***N*-(3-ethyl-3'-phenyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)benzenesulfonamide (4m)**

White solid, 69.4 mg, 70% yield; mp: 156-157 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79-7.73 (m, 2H), 7.60-7.54 (m, 3H), 7.50-7.40 (m, 4H), 7.36-7.28 (m, 5H), 7.10 (dd, *J* = 2.0, 1.2 Hz, 1H), 6.76-6.73 (m, 1H), 6.64 (s, 1H), 6.60-6.51 (m, 2H), 4.14 (t, *J* = 7.4 Hz, 1H), 2.08-1.98 (m, 2H), 0.92 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.0, 149.4, 138.9, 134.2, 133.0, 131.9, 131.0, 129.9, 129.4, 129.0, 128.5, 127.5, 127.0, 125.4, 125.2, 12.0, 124.7, 121.0, 112.2, 110.3, 100.4, 50.5, 21.5, 12.7. HRMS (ESI) *m/z*: calcd for $[C_{30}H_{26}NO_4S]^+$ requires: 496.1583 $[M+H]^+$; found: 496.1582.

4-methyl-*N*-(3'-phenyl-3-propyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)benzenesulfonamide (4n)

White solid, 73.3 mg, 70% yield; mp: 161-162 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64-7.62 (m, 2H), 7.60-7.56 (m, 2H), 7.49-7.47 (m, 1H), 7.44-7.40 (m, 1H), 7.36-7.28 (m, 5H), 7.28-7.25 (m, 2H), 7.10 (s, 1H), 6.71 (dd, *J* = 8.3, 1.8 Hz, 1H), 4.25-4.19 (m, 1H), 2.40 (s, 3H), 2.02-1.89 (m, 2H), 1.35-1.25 (m, 2H), 0.86 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.0, 149.4, 143.8, 136.0, 134.2, 132.0, 131.1, 129.9, 129.6, 129.0, 128.5, 127.6, 127.0, 126.8, 125.4, 125.1, 125.0, 124.7, 121.0, 112.3, 110.2, 100.4, 48.8, 30.6, 21.7, 21.3, 14.5. HRMS (ESI) *m/z*: calcd for $[C_{32}H_{30}NO_4S]^+$ requires: 524.1896 $[M+H]^+$; found: 524.1893.

***N*-(3'-phenyl-3-propyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)benzenesulfonamide (4o)**

White solid, 77.5 mg, 76% yield; mp: 195-196 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78-7.76 (m, 2H), 7.59-7.55 (m, 3H), 7.50-7.40 (m, 4H), 7.37-7.27 (m, 5H), 7.11 (s, 1H), 6.75-6.73 (m, 1H), 6.64 (s, 2H), 6.56 (d, *J* = 8.4 Hz, 1H), 4.27-4.15 (m, 1H), 2.05-1.87 (m, 2H), 1.32 (tt, *J* = 13.6, 6.7 Hz, 2H), 0.85 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.0, 149.4, 138.9, 134.2, 133.0, 132.0, 131.1, 129.9, 129.5, 129.0, 128.5, 127.5, 127.0, 126.8, 125.4, 125.1, 125.0, 124.7, 121.0, 112.3, 110.3, 100.4, 48.8, 30.5, 21.3, 14.5. HRMS (ESI) *m/z*: calcd for $[C_{31}H_{28}NO_4S]^+$ requires: 510.1739 $[M+H]^+$; found: 510.1741.

4-chloro-*N*-(3'-phenyl-3-propyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)benzenesulfonamide (4p)

White solid, 77.3 mg, 71% yield; mp: 194-195 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68-7.65 (m, 2H), 7.60-7.55 (m, 2H), 7.49 (d, *J* = 7.9 Hz, 1H), 7.46-7.40 (m, 3H), 7.37-7.28 (m, 5H), 7.09 (s, 1H), 6.76-6.70 (m, 1H), 6.64 (s, 1H), 6.58 (d, *J* = 8.4 Hz, 1H), 6.40 (s, 1H), 4.23 (dd, *J* = 8.2, 6.1 Hz, 1H), 2.05-1.90 (m, 2H), 1.33 (qd, *J* = 13.9, 7.2 Hz, 2H), 0.87 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 149.4, 139.6, 137.4, 134.2, 132.2, 131.1, 129.9, 129.3, 129.1, 128.9, 128.5, 127.0, 126.7, 125.38 (d, *J* = 11.9 Hz), 125.0, 124.7, 121.2, 112.3, 110.4, 100.5, 48.8, 30.6, 21.3, 14.5. HRMS (ESI) *m/z*: calcd for $[C_{31}H_{27}ClNO_4S]^+$ requires: 544.1349 $[M+H]^+$; found: 544.1344.

***N*-(3'-phenyl-3-propyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)naphthalene-2-sulfonamide (4q)**

White solid, 80.3 mg, 72% yield; mp: 201-202 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.00 (s, 1H), 8.33 (s, 1H), 8.09-8.07 (m, 2H), 7.99 (d, *J* = 8.1 Hz, 1H), 7.76 (dd, *J* = 8.7, 1.6 Hz, 1H), 7.65-7.59 (m, 3H), 7.47-7.45 (m, 2H), 7.40 (t, *J* = 7.4 Hz, 1H), 7.32-7.28 (m, 4H), 7.24-7.22 (m, 1H), 6.98 (s, 1H), 6.88 (s, 1H), 6.81 (dd, *J* = 8.4, 1.7 Hz, 1H), 6.51 (d, *J* = 8.4 Hz, 1H), 4.30 (dd, *J* = 8.3, 5.9 Hz, 1H), 2.50-2.41 (m, 2H), 1.75-1.58 (m, 2H), 1.09 (ddt, *J* = 20.5, 13.0, 6.3 Hz, 2H), 0.67 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 153.6, 148.6, 136.9, 134.8, 134.1, 132.1, 131.9, 131.5, 131.1, 130.3, 129.8, 129.7, 129.5, 129.4, 129.2, 128.6, 128.4, 128.2, 127.5, 127.0, 125.6, 124.8, 123.4, 122.8, 119.2, 112.1, 110.0, 100.9, 47.9, 30.5, 21.0, 14.7. HRMS (ESI) *m/z*: calcd for $[C_{35}H_{30}NO_4S]^+$ requires: 560.1896 $[M+H]^+$; found: 560.1893.

***N*-(3-isopropyl-3'-phenyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)-4-methylbenzenesulfonamide (4r)**

White solid, 78.6 mg, 75% yield; mp: 202-203 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67-7.59 (m, 4H), 7.42-7.33 (m, 5H), 7.29-7.27 (m, 1H), 7.26-7.24 (m, 2H), 7.16 (d, *J* = 1.1 Hz, 1H), 6.75 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.65 (s, 1H), 6.55 (d, *J* = 8.4 Hz, 1H), 6.28 (s, 1H), 4.02 (d, *J* = 5.5 Hz, 1H), 2.51 (dq, *J* = 13.7, 6.8 Hz, 1H), 2.40 (s, 3H), 1.08 (d, *J* = 6.7 Hz, 3H), 1.00 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.4, 149.5, 143.9, 136.0, 134.1, 130.5, 130.0, 129.8, 129.6, 129.1, 129.0, 128.5, 127.9, 127.6, 127.1, 125.5, 125.4, 125.1, 124.3, 122.2, 112.6, 110.3, 100.6, 55.0, 27.6, 22.3, 21.6, 20.3. HRMS (ESI) *m/z*: calcd for $[C_{32}H_{30}NO_4S]^+$ requires: 524.1896 $[M+H]^+$; found: 524.1897.

4-methyl-*N*-(3'-phenyl-3-(p-tolyl)-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)benzenesulfonamide (4s)

White solid, 78.9 mg, 69% yield; mp: 213-214 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.5 Hz, 1H), 7.63-7.61 (m, 2H), 7.44-7.34 (m, 4H), 7.32-7.26 (m, 4H), 7.26-7.21 (m, 2H), 7.07 (d, *J* = 8.1 Hz, 2H), 7.02-6.93 (m, 3H), 6.87 (s, 1H), 6.72 (d, *J* = 8.4 Hz, 1H), 6.51 (s, 1H), 6.44 (s, 1H), 5.42 (s, 1H), 2.43 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 149.6, 143.8, 137.4, 136.0, 134.0, 131.9, 131.8, 130.5, 130.0, 129.9, 129.7, 128.9, 128.8, 128.3, 127.6, 127.1, 126.2, 125.7, 125.4, 124.9, 124.7, 122.0, 112.5, 110.7, 100.3, 56.2, 21.7, 21.2. HRMS (ESI) *m/z*: calcd for $[C_{36}H_{30}NO_4S]^+$ requires: 572.1896 $[M+H]^+$; found: 572.1895.

***N*-(3-(4-chlorophenyl)-3'-phenyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)-4-methylbenzenesulfonamide (4t)**

White solid, 83.0 mg, 70% yield; mp: 174-175 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65-7.63 (m, 1H), 7.60 (d, *J* = 8.1 Hz, 2H), 7.44-7.40 (m, 1H), 7.38-7.33 (m, 3H), 7.30-7.26 (m, 3H), 7.25-7.20 (m, 3H), 7.13 (d, *J* = 8.3 Hz, 2H), 7.08 (d, *J* = 8.4 Hz, 2H), 6.97-6.92 (m, 1H), 6.84 (s, 1H), 6.73 (d, *J* = 8.4 Hz, 1H), 6.42 (d, *J* = 5.6 Hz, 2H), 5.38 (s, 1H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 149.6, 143.9, 136.0, 133.8, 133.7, 133.6, 131.6, 131.3, 130.2, 130.0, 129.8, 129.7, 129.0, 128.4, 128.3, 127.5, 127.2, 126.0, 125.4, 124.8, 124.5, 121.8, 112.4, 110.9, 100.3, 56.3, 21.7.HRMS (ESI) *m/z*: calcd for $[C_{35}H_{27}ClNO_4S]^+$ requires: 592.1349 $[M+H]^+$; found: 592.1345.

***N*-(3-(4-bromophenyl)-3'-phenyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)-4-methylbenzenesulfonamide (4u)**

White solid, 91.5 mg, 72% yield; mp: 161-162 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65-7.63 (m, 1H), 7.62-7.60 (m, 2H), 7.45-7.41 (m, 1H), 7.39-7.34 (m, 3H), 7.31-7.28 (m, 5H), 7.25-7.22 (m, 2H), 7.03 (dd, *J* = 8.7, 2.0 Hz, 2H), 6.95 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.86 (d, *J* = 12.3 Hz, 1H), 6.76-6.71 (m, 1H), 6.43 (d, *J* = 6.0 Hz, 2H), 5.37 (s, 1H), 2.43 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 149.6, 143.9, 136.0, 134.2, 133.8, 131.7, 131.6, 131.4, 130.2, 130.0, 129.7, 129.0, 128.4, 127.5, 127.2, 126.0, 125.4, 124.8, 124.5, 121.8, 112.4, 110.9, 100.4, 56.4, 21.7. HRMS (ESI) *m/z*: calcd for $[C_{35}H_{27}BrNO_4S]^+$ requires: 636.0844 $[M+H]^+$; found: 636.0842.

4-methyl-*N*-(3-phenyl-3'-(p-tolyl)-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)benzenesulfonamide (4v)

White solid, 67.5 mg, 59% yield; mp: 173-174 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.68 (m, 1H), 7.61-7.59 (m, 2H), 7.45-7.34 (m, 4H), 7.30-7.26 (m, 4H), 7.25-7.23 (m, 1H), 7.22-7.17 (m, 1H), 7.08-7.06 (m, 2H), 6.99 (d, *J* = 8.0 Hz, 2H), 6.96-6.94 (m, 1H), 6.86 (s, 1H), 6.72 (d, *J* = 8.4 Hz, 1H), 6.44 (s, 1H), 6.27 (s, 1H), 5.42 (s, 1H), 2.43 (s, 3H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 149.6, 143.8, 137.5, 136.0, 134.0, 131.8, 130.6, 130.0, 129.8, 129.6, 128.9, 128.3, 127.5, 127.1, 126.2, 125.8, 125.4, 124.9, 124.6, 122.1, 112.5, 110.7, 100.3, 56.1, 21.7, 21.2. HRMS (ESI) *m/z*: calcd for $[C_{36}H_{29}NO_4SNa]^+$ requires: 594.1715 $[M+Na]^+$; found: 594.1721.

***N*-(3'-(3-fluorophenyl)-3-phenyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)-4-methylbenzenesulfonamide (4w)**

White solid, 54.1 mg, 47% yield; mp: 174-175 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.5 Hz, 1H), 7.60 (d, *J* = 8.3 Hz, 2H), 7.42 (td, *J* = 7.4, 1.4 Hz, 1H), 7.37 (td, *J* = 7.5, 1.5 Hz, 1H), 7.27 (s, 1H), 7.25 (s, 1H), 7.22 (d, *J* = 1.0 Hz, 1H), 7.21-7.14 (m, 5H), 7.11 (dd, *J* = 7.7, 1.7 Hz, 2H), 7.01-6.91 (m, 3H), 6.86 (s, 1H), 6.74 (d, *J* = 8.4 Hz, 1H), 6.40 (d, *J* = 4.5 Hz, 2H), 5.40 (s, 1H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 155.8, 148.30 (d, *J* = 2.9 Hz), 143.9, 136.22 (d, *J* = 8.2 Hz), 135.9, 135.0, 131.2, 130.1 (d, *J* = 3.0Hz), 128.3, 127.9, 127.56 (d, *J* = 3.1 Hz), 126.5, 125.9, 125.5, 124.7, 122.0, 120.4 (d, *J* = 2.9 Hz), 115.7, 115.4, 112.5, 111.9, 111.7, 110.7, 101.1, 77.37 (d, *J* = 11.4 Hz), 77.1, 76.8, 60.5, 57.0, 21.7, 21.2, 14.3. HRMS (ESI) *m/z*: calcd for $[C_{35}H_{26}FNO_4SNa]^+$ requires: 598.1464 $[M+Na]^+$; found: 598.1473.

***N*-(3,3'-diphenyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)-4-methylbenzenesulfonamide (4x)**

White solid, 59.1 mg, 53% yield; mp: 217-218 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.6 Hz, 1H), 7.61 (d, *J* = 8.2 Hz, 2H), 7.45-7.41 (m, 1H), 7.40-7.34 (m, 3H), 7.30-7.23 (m, 6H), 7.22-7.16 (m, 5H), 6.96 (dd, *J* = 8.5, 1.2 Hz, 1H), 6.88 (s, 1H), 6.73 (d, *J* = 8.4 Hz, 1H), 6.42 (s, 2H), 5.44 (s, 1H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 149.6, 143.8, 136.0, 135.1, 133.9, 131.7, 130.2, 130.1, 130.0, 129.9, 129.7, 128.8, 128.3, 128.2, 127.8, 127.6, 127.1, 126.2, 125.8, 125.3, 124.9, 122.0, 112.6, 110.7, 100.2, 56.8, 21.7.HRMS (ESI) *m/z*: calcd for $[C_{35}H_{27}NO_4SNa]^+$ requires: 580.1558 $[M+Na]^+$; found: 580.1553.

***N*-(3,3'-diphenyl-3*H*-spiro[benzofuran-2,1'-isochromen]-5-yl)benzenesulfonamide (4y)**

White solid, 62.0 mg, 57% yield; mp: 174-175 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79-7.72 (m, 2H), 7.69 (d, *J* = 7.6 Hz, 1H), 7.63-7.57 (m, 1H), 7.50-7.40 (m, 3H), 7.40-7.34 (m, 3H), 7.31-7.26 (m, 3H), 7.24-7.12 (m, 6H), 7.02-6.99 (m, 1H), 6.86 (dd, *J* = 2.1, 1.2 Hz, 1H), 6.74 (d, *J* = 8.5 Hz, 1H), 6.64 (s, 1H), 6.43 (s, 1H), 5.44 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0, 149.6, 138.8, 135.0, 133.9, 133.0, 131.7, 130.3, 130.1, 130.0, 129.7, 129.1, 128.9, 128.3, 128.2, 127.8, 127.5, 127.1, 125.9, 125.4, 124.9, 124.7, 122.0, 112.6, 110.8, 100.3, 56.6. HRMS (ESI) *m/z*: calcd for $[C_{34}H_{26}NO_4S]^+$ requires: 544.1583 $[M+H]^+$; found: 544.1581.

4-chloro-N-(3,3'-diphenyl-3H-spiro[benzofuran-2,1'-isochromen]-5-yl)benzenesulfonamide (4z)

White solid, 63.6 mg, 55% yield; mp: 192-193 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.3 Hz, 1H), 7.67-7.61 (m, 2H), 7.47-7.41 (m, 3H), 7.40-7.34 (m, 3H), 7.32-7.26 (m, 3H), 7.26-7.20 (m, 4H), 7.18-7.10 (m, 2H), 7.02-6.99 (m, 1H), 6.81 (dd, *J* = 2.1, 1.2 Hz, 1H), 6.76 (d, *J* = 8.5 Hz, 1H), 6.44 (d, *J* = 11.8 Hz, 2H), 5.44 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.2, 149.6, 139.6, 137.3, 134.9, 133.9, 131.7, 130.5, 130.1, 129.32 (d, *J* = 3.7 Hz), 129.0), 128.3, 127.9, 127.1, 126.1, 125.4, 124.8, 124.6, 122.1, 112.6, 110.9, 100.3, 56.7, 31.0. HRMS (ESI) *m/z*: calcd for $[C_{34}H_{25}ClNO_4S]^+$ requires: 578.1193 $[M+H]^+$; found: 578.1190.

4-chloro-N-(3-(4-chlorophenyl)-3'-phenyl-3H-spiro[benzofuran-2,1'-isochromen]-5-yl)benzenesulfonamide (4aa)

White solid, 50.2 mg, 41% yield; mp: 201-202 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.96 (s, 1H), 7.97 (d, *J* = 7.7 Hz, 1H), 7.68-7.55 (m, 4H), 7.41 (t, *J* = 7.4 Hz, 1H), 7.35-7.26 (m, 7H), 7.05 (d, *J* = 8.4 Hz, 2H), 6.95 (d, *J* = 8.4 Hz, 1H), 6.77 (s, 1H), 6.71 (d, *J* = 8.5 Hz, 1H), 6.62 (s, 1H), 5.85 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 154.7, 148.6, 138.3, 134.7, 133.8, 132.9, 132.2, 131.9, 131.4, 130.7, 130.5, 129.7, 129.4, 129.1, 128.7, 127.8, 126.1, 125.5, 124.7, 120.1, 112.3, 110.9, 101.2, 53.8. HRMS (ESI) *m/z*: calcd for $[C_{34}H_{24}Cl_2NO_4S]^+$ requires: 612.0803 $[M+H]^+$; found: 612.0801.

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FULL PAPER

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