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Metal-Free Oxidative Spirocyclization of Alkynes with Sulfonylhydrazides Leading to 3-Sulfonated Azaspiro[4,5]trienones

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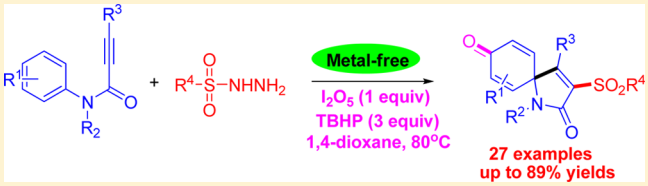
Supporting Information

ABSTRACT: A novel and direct oxidative spirocyclization of arylpropiolamides with sulfonylhydrazides leading to 3-sulfonated azaspiro[4,5]trienones has been developed under metal-free conditions. The reaction is performed in a tandem manner constituted by the sequential sulfonylation of alkynes, *ipso*-carbocyclization, dearomatization, hydration, and oxidation processes, providing a convenient and efficient approach to various sulfonated azaspiro[4,5] trienones of biological importance.



INTRODUCTION

The spirocyclic molecular framework is a prevalent feature for various natural products, pharmaceuticals, and functional materials.[1] Spirocycles as versatile building blocks have also been broadly utilized for constructing various complex and highly valuable organic compounds.[2] Particularly, azaspirocyclohexadienones have recently attracted considerable synthetic attention due to their interesting biological activities[3] and important synthetic applications[4] (Figure 1). Consequently, substantial efforts have been devoted to the synthesis of azaspirocyclo-hexadienones. In general, traditional approaches are mainly focused on intramolecular cyclization reactions such as electrophilic substitution on *N*-acyliminium or thionium ions,[5] radical *ipso*-carbocyclization,[6] *ipso*-Friedel−Crafts/Michael addition cascade reactions,[7] or transition-metal-catalyzed intramolecular dearomatization strategy.[8] Nevertheless, most of these methods suffer from some limitations such as unreadily available starting materials, tedious workup procedures, harsh reaction conditions, and/or the use of expensive metal-catalysts (i.e., Pd, Au, Ir and Ru). Moreover, most of the current methods focus only on the improvement of the pre-existing frameworks, with no new functional groups incorporated into the products. Recently, the difunctionalization of alkynes as the powerful and fascinating protocol has attracted considerable attention of chemists because it could provide an efficient way to form new carbon−carbon and carbon−heteroatom bonds in a single operation.[9] Through this methodology, many useful functional groups could be successfully introduced into organic frameworks. Nevertheless, up to date, only few strategies have been developed to construct substituted spirocyclohexadienones via the difunctionalization of alkynes such as *ipso*-carbohalogenation, carbothiocyanation, carboalkylation, carboacylation, and carbonphosphonation.[10,11] It is still a challenging but attractive task to develop direct, convenient, efficient, and environmentally benign reaction system to afford a variety of important and structurally diverse functional spirocyclohexadienones.

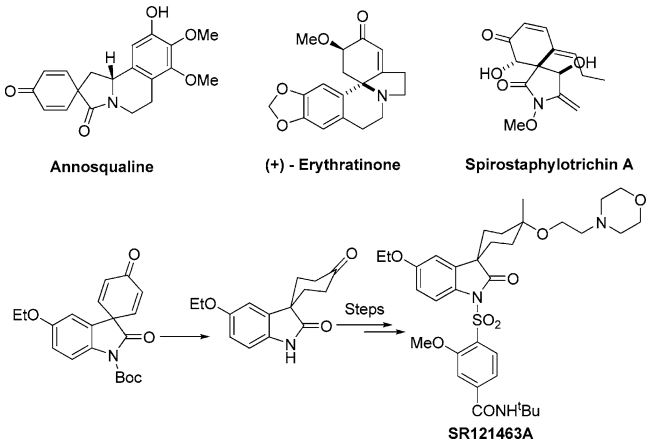


Figure 1. Representative azaspirocycle-based nature products and synthetic applications.

Sulfone groups represent one kind of the most important classes of organic functionalities, which are widely found in a number of biologically active compounds, drug molecules, and versatile synthetic intermediates.[12] As a result, the development of novel and efficient synthetic methods for the introduction of the sulfone groups into organic frameworks has concentrated much interest of chemists in both academic and industrial laboratories.[13] In the continuation of our efforts in constructing sulfone-containing compounds,[14] here, we wish to report a new and direct oxidative spirocyclization of alkynes with sulfonylhydrazides toward 3-sulfonated azaspiro[4,5]trienones in the presence of I_2O_5/TBHP system (Scheme 1). The present protocol offers a convenient and efficient approach to a series

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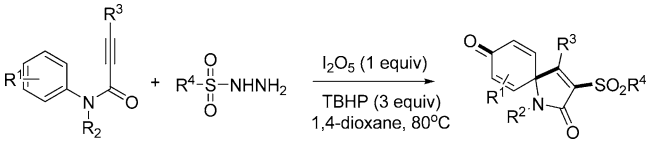
Scheme 1. Oxidative Spirocyclization of Alkynes with Sulfonylhydrazides

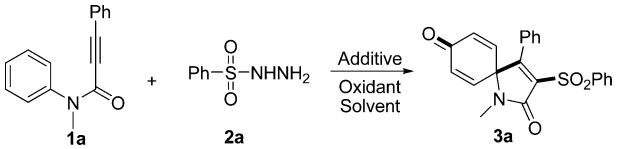


of 3-sulfonated azaspiro[4,5]trienones in moderate to high yields by the sequential C−S, C−C, and C═O bond formation under metal-free reaction conditions.

RESULTS AND DISCUSSION

In an initial experiment, *N*-methyl-*N*,3-diphenylpropiolamide **1a** and phenylsulfonohydrazide **2a** were chosen as the model substrates to optimize the reaction conditions. To our delight, the desired sulfonated azaspiro[4,5]trienone **3a** was obtained in 40% yield when the reaction was carried out by using I_2 (1 equiv) and TBHP (3 equiv) in 1,4-dioxane at 80 °C (Table 1, entry 1). The structure of **3a** was unambiguously conformed by single-crystal X-ray analysis (Figure 2). The screening of various additives found that I_2O_5 was the optimized one for mediating the formation of product **3a** (Table 1, entries 1−6).

Table 1. Optimization of the Reaction Conditions[a]



entry	additive	oxidant	yield (%)[b]
1	I_2	TBHP	40
2	NaI	TBHP	22
3	TBAI	TBHP	trace
4	TBAB	TBHP	0
5	TBAF	TBHP	0
6	I_2O_5	TBHP	89
7	$AgNO_3$	TBHP	32
8	$Cu(OAc)_2$	TBHP	13
9	$FeCl_3·6H_2O$	TBHP	20
10	I_2O_5	DTBP	62
11	I_2O_5	H_2O_2	52
12	I_2O_5	$K_2S_2O_8$	62
13	I_2O_5	$(NH_4)S_2O_8$	59
14	I_2O_5	$Na_2S_2O_8$	52
15	I_2O_5	Oxone	70
16	I_2O_5	Air(O_2)	43
17	I_2O_5	TBHP	40[c]
18	I_2O_5	TBHP	54[d]
19	I_2O_5	TBHP	66[e]
20	I_2O_5	TBHP	45[f]
21	I_2O_5	TBHP	64[g]
22	I_2O_5	-	11
23	-	TBHP	trace

[a]Reaction conditions: **1a** (0.25 mmol), **2a** (0.75 mmol), additive (1 equiv), oxidant (3 equiv), solvent (2 mL), 80 °C, 12 h. TBHP: *tert*-Butyl hydroperoxide, 70% solution in water; TBAI = $(n\text{-Bu})_4NI$; TBAB = $(n\text{-Bu})_4NBr$; TEAF = $(n\text{-Bu})_4NF$; DTBP: Di-*tert*-butyl peroxide; Oxone: Potassium peroxymonosulfate. [b]Isolated yields based on **1a**. [c]I_2O_5 (0.5 equiv). [d]TBHP (1 equiv). [e]TBHP (2 equiv). [f]25 °C. [g]60 °C.

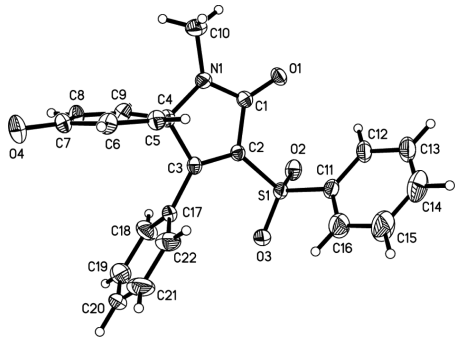


Figure 2. Crystal structure of **3a**. ORTEP drawing of $C_{22}H_{17}NO_4S$ with 30% probability ellipsoids, showing the atomic numbering scheme.

Replacing of I_2O_5 with metal additives such as Ag, Cu, and Fe salts did not improve yields (Table 1, entries 7−9). Further optimization of various oxidants indicated that TBHP was the best choice, whereas the others like DTBP, H_2O_2, $K_2S_2O_8$, $(NH_4)_2S_2O_8$, $Na_2S_2O_8$, Oxone, and O_2 were less effective (Table 1, entries 10−16). Also, among the solvents tested, 1,4-dioxane and DME were shown to be more effective than the others such as DCE, CH_3OH, toluene, CH_3CN, and H_2O (see Table S1 in the Supporting Information). Moreover, no conversion was observed when the reaction was performed separately in DMF and DMSO (see Table S1 in the Supporting Information). In addition, the reaction efficiency was obviously low with the decreasing of I_2O_5 or TBHP loading or reaction temperature (Table 1, entries 17−21). The desired product was obtained in 11% yield when the model reaction was performed in the presence of I_2O_5 and only a trace amount of product was detected when reaction conducted in the presence of TBHP (Table 1, entries 22−23). After an extensive screening of the reaction parameters, the best yield of **3a** (89%) was obtained by employing of I_2O_5 (1 equiv) and TBHP (3 equiv) in 1,4-dioxane at 80 °C (Table 1, entry 6).

Under the optimized conditions, the scope and limitations of this new oxidative spirocyclization reaction were explored, with some results summarized in Table 2. Generally, the reaction could proceed well by using diverse arylsulfonohydrazides with an electron-donating group (Me or MeO) or an electron-withdrawing group (Cl, Br, or CF_3) on the aromatic ring so as to afford the corresponding products in moderate to good yields (**3a**−**3f**). Subsequently, substituent effects on the alkynyl moiety were examined. Arylalkynes bearing both of the electron-donating and electron-withdrawing groups on the aromatic moieties were tolerated in this reaction to give the desired products in good yields (**3g**−**3k**). As expected, the reaction also worked well with alkylalkyne, obtaining the corresponding product **3l** in 60% yield. Nevertheless, changing the N-Me group to a N−H, or N−Ac group failed to yield the desired product (**3m** or **3n**), which might be caused by the electronic effect[10b,11b,c] Finally, *N*-arylpropiolamides with various substitution patterns at the aniline moieties were tested. It was found that the reaction was not significantly affected by the steric effect. Herein, the ortho- or meta-position of the aniline moieties were suitable for this reaction, with the desired products obtained in good yields (**3o**−**3x**). Interestingly, the para-position substituted *N*-arylpropiolamides could give the corresponding spiro[4,5]trienone **3a** in good yields by releasing the para-substituents (*p*-MeO−, *p*-F, and *p*-I) (eq 1).[11]

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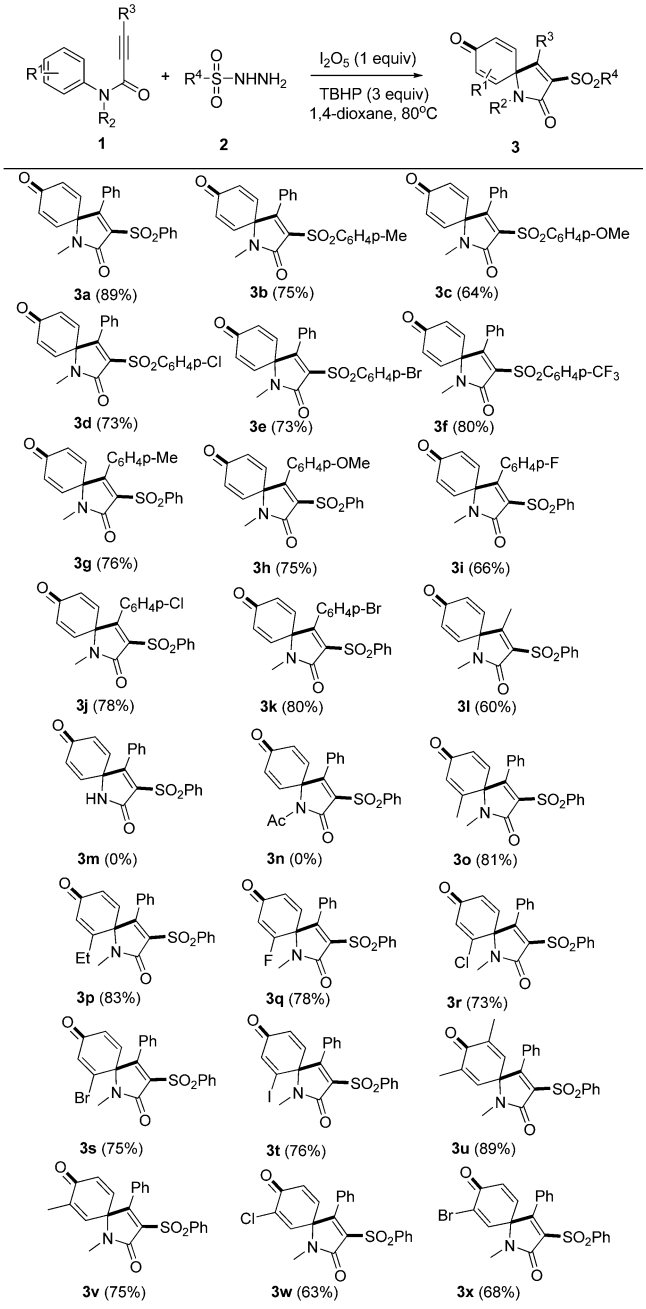
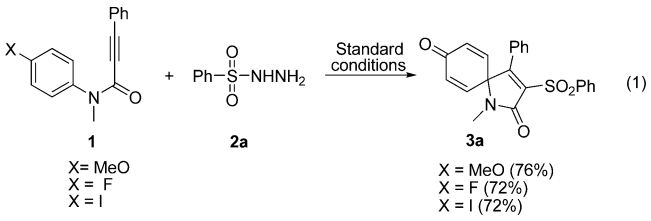
Table 2. Results for the Metal-Free Oxidative Spirocyclization of Alkynes with Sulfonylhydrazides[a,b]



[a]Reaction conditions: **1** (0.25 mmol), **2** (0.75 mmol), I_2O_5 (1 equiv), TBHP (3 equiv), 1,4-dioxane (2 mL), 80 °C, 12−30 h. [b]Isolated yields based on **1**.



Furthermore, to demonstrate the potential synthetic application of the present method, we point out that sulfonated azaspiro[4,5]trienone **3** can be transformed into some valuable synthons through conventional organic reactions such as transition metal−catalyzed Heck reactions,[11c] Michael addition reactions,[15a] and hydrogenation reactions[15b] (Scheme 2).

Several control experiments were further performed to gain an insight into the reaction mechanism. The results are shown in Scheme 3. Accordingly, when *N*-methyl-*N*,3-diphenylpropiolamide **1a** was performed dependently under the standard conditions, azaspiro[4,5]trienone **A** could not form (eq 2, Scheme 3). This result indicated that azaspiro[4,5]trienone **A** might not be the key intermediate in this reaction. Moreover, the oxidative spirocyclization reaction was completely inhibited when 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO, a well-known radical scavenger) was added into the present reaction system, suggesting the reaction presumably underwent a radical pathway (eq 3, Scheme 3). Further investigation found that the model reaction could be extremely inhibited when 4 Å MS was introduced into the reaction system (eq 4, Scheme 3). Also, ^{18}O atom could be incorporated in the corresponding spiro[4,5]trienone **3a** when the reaction of **1a** with **2a** was performed in the presence of $H_2{}^{18}O$ (eq 5, Scheme 3). These results clearly demonstrated that the carbonyl oxygen atom came from water. In addition, the intermolecular kinetic isotope effect (KIE) experiment was observed with k_H/k_D = 1.0, which indicated that C−H bond cleavage might not be the rate-determining step in the present transformation (eq 6, Scheme 3).

On the basis of the above results and previous reports,[6,7,12−17] a possible reaction pathway was proposed and described in Scheme 4. Initially, the single-electron oxidation of sulfonylhydrazide **2** mediated by I_2O_5 would form sulfonyl radical **4** and I_2. The generation of molecular iodine could be confirmed by observation of an obvious color change from reddish brown to deep blue when starch was added into the present reaction system.[16] Next, the selective addition of sulfonyl radical **4** to arylpropiolamide **1** gave the vinyl radical **5**. Furthermore, intramolecular *spiro*-cyclization of vinyl radical **5** with an aryl ring generated the radical intermediate **6**, which produced the corresponding cyclohexadienyl cation **7** via a single-electron-transfer process.[17] Subsequently, the nucleophilic attack of H_2O to cation **7** afforded intermediate **8**, which was detected by LC−MS (see Supporting Information).[18] Finally, oxidation of intermediate **8** by TBHP would lead to the formation of the desired sulfonated azaspiro[4,5]trienone **3**.

CONCLUSIONS

In conclusion, a simple and metal-free protocol has been successfully developed for the synthesis of sulfonated azaspiro[4,5]trienones through I_2O_5-mediated direct oxidative spirocyclization of arylpropiolamides with sulfonylhydrazides. This tandem reaction is constituted by the sequential sulfonylation of alkynes, *ipso*-carbocyclization, dearomatization, hydration, and oxidation processes. The as-developed protocol provides a convenient and efficient approach to various biologically important sulfonated azaspiro[4,5]trienones in moderate to good yields.

EXPERIMENTAL SECTION

General. Chemicals were commercially available and were used without further purification unless otherwise stated. All solvents were used as received without further purification unless otherwise stated. ^1H NMR and ^{13}C NMR spectra were obtained in $CDCl_3$ with TMS as internal standard (400 MHz ^1H and 100 MHz ^{13}C) at room temperature; the chemical shifts (δ) were expressed in ppm and *J*

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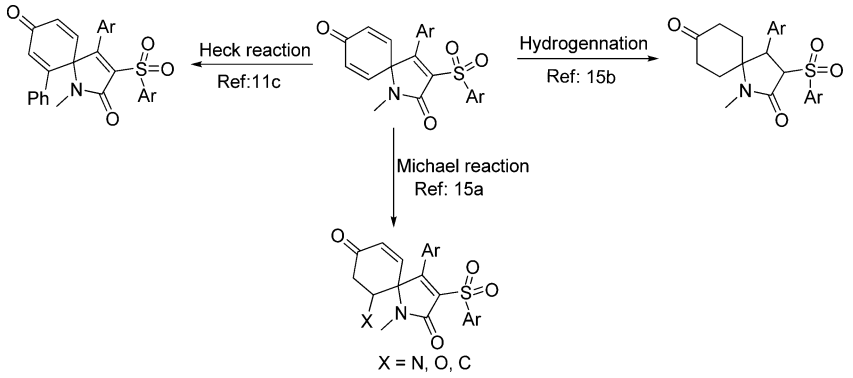
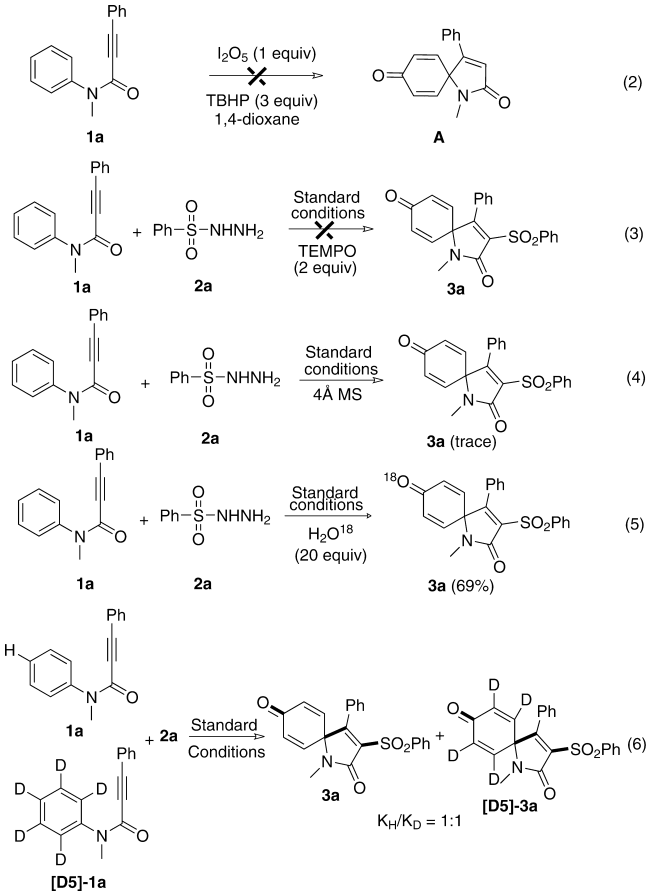
Scheme 2. Potential Synthetic Applications of Sulfonated Azaspiro[4,5]trienone



Scheme 3. Preliminary Mechanistic Studies



values were given in Hz. The following abbreviations are used to indicate the multiplicity: singlet (s), doublet (d), triplet (t), quartet (q), doublet of doublets (dd), doublet of triplets (dt), doublet of quartets (dq) and multiplet (m). All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted were designated as multiplet (m). In a few cases, the number of signals in the ^{13}C NMR spectrum is than due, which may be caused by the superimposition of signals. HRMS data were obtained by ESI on a TOF mass analyzer. Column chromatography was performed on silica gel (200−300 mesh). All *N*-arylpropiolamides **1** were synthesized according to the known procedures.[19]

General Experimental Procedures. To a mixture of *N*-arylpropiolamides **1** (0.25 mmol), sulfonylhydrazides **2** (0.75 mmol), I_2O_5 (0.25 mmol), and TBHP (0.75 mmol) in a 25 mL round-bottomed flack at room temperature was added the 1,4-dioxane (2 mL). The reaction vessel was allowed to stir at 80 °C for 12−30 h. After the reaction, the solvent was then removed under vacuum. The residue was purified by flash column chromatography using a mixture of petroleum ether and ethyl acetate as eluent to give the desired product **3**.

*1-Methyl-4-phenyl-3-(phenylsulfonyl)-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione (**3a**).* Compound **3a** was obtained in 89% yield (87 mg) according to the general procedure (12 h); yellow solid; mp 206.5−208.3 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 7.5 Hz, 2H), 7.68 (t, J = 7.4 Hz, 1H), 7.57 (t, J = 7.7 Hz, 2H), 7.46 (t, J = 7.4 Hz, 1H), 7.39 (t, J = 7.4 Hz, 2H), 7.17 (d, J = 7.2 Hz, 2H), 6.46 (s, 4H), 2.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.1, 163.5, 162.2, 142.2, 139.2, 136.7, 134.4, 130.4, 129.2, 129.1, 128.5, 128.0, 127.8, 68.3, 26.4. HRMS (ESI) calcd for $C_{22}H_{17}NO_4NaS$ $(M + Na)^+$ 414.0776, found 414.0778.

*1-Methyl-4-phenyl-3-tosyl-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione (**3b**).* Compounds **3b** were obtained in 75% yield (80 mg) according to the general procedure (30 h); yellow solid; mp 283.0−286.4 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.3 Hz, 2H), 7.46 (t, J = 7.4 Hz, 1H), 7.41−7.35 (m, 4H), 7.16 (d, J = 7.1 Hz, 2H), 6.46 (s, 4H), 2.84 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.1, 163.6, 161.6, 145.6, 142.3, 136.9, 136.1, 134.3, 130.4, 129.8, 129.3, 128.6, 128.0, 127.8, 68.3, 26.4, 21.8; HRMS (ESI) calcd for $C_{23}H_{19}NO_4NaS$ $(M + Na)^+$ 428.0932, found 428.0929.

*3-(4-Methoxyphenylsulfonyl)-1-methyl-4-phenyl-1-azaspiro[4.5]-deca-3,6,9-triene-2,8-dione (**3c**).* Compound **3c** was obtained in 64% yield (67.4 mg) according to the general procedure (30 h); orange solid; mp 216.6−218.7 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 8.8 Hz, 2H), 7.44 (t, J = 7.4 Hz, 1H), 7.38 (t, J = 7.6 Hz, 2H), 7.15 (d, J = 7.2 Hz, 2H), 7.01 (d, J = 8.9 Hz, 2H), 6.46 (s, 4H), 3.89 (s, 3H), 2.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.2, 164.4, 163.8, 161.0, 142.4, 137.1, 134.3, 131.6, 130.4, 130.3, 128,7, 128.0, 127.9, 114.3, 68.3, 55.7, 26.4; HRMS (ESI) calcd for $C_{23}H_{19}NO_5NaS$ $(M + Na)^+$ 444.0882, found 444.0883.

*3-(4-Chlorophenylsulfonyl)-1-methyl-4-phenyl-1-azaspiro[4.5]-deca-3,6,9-triene-2,8-dione (**3d**).* Compound **3d** was obtained in 73% yield (77.6 mg) according to the general procedure (30 h); yellow solid; mp 258.5−260.5 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.7 Hz, 2H), 7.54 (d, J = 8.7 Hz, 2H), 7.48 (t, J = 7.5 Hz, 1H), 7.42−7.38 (m, 2H), 7.17 (d, J = 7.2 Hz, 2H), 6.47 (d, J = 1.2 Hz, 4H), 2.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.0, 163.4, 162.4, 144.1, 142.0, 141.3, 137.5, 134.5, 133.3, 130.8, 130.6, 129.4, 128.1, 127.8, 68.4, 26.4; HRMS (ESI) calcd for $C_{22}H_{16}ClNO_4NaS$ $(M + Na)^+$ 448.0386, found 448.0390.

*3-(4-Bromophenylsulfonyl)-1-methyl-4-phenyl-1-azaspiro[4.5]-deca-3,6,9-triene-2,8-dione (**3e**).* Compounds **3e** were obtained in 73% yield (85.6 mg) according to the general procedure (30 h); white solid; mp 231.1−233.8 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.7 Hz, 2H), 7.70 (d, J = 8.7 Hz, 2H), 7.47 (t, J = 7.4 Hz, 1H), 7.40 (t, J = 7.5 Hz, 2H), 7.16 (d, J = 7.1 Hz, 2H), 6.47 (s, 4H), 2.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.0, 163.5, 162.5, 144.1, 142.0, 138.0, 136.3, 134.5, 133.3, 132.4, 130.8, 130.6, 128.1, 127.8, 68.4, 26.4;

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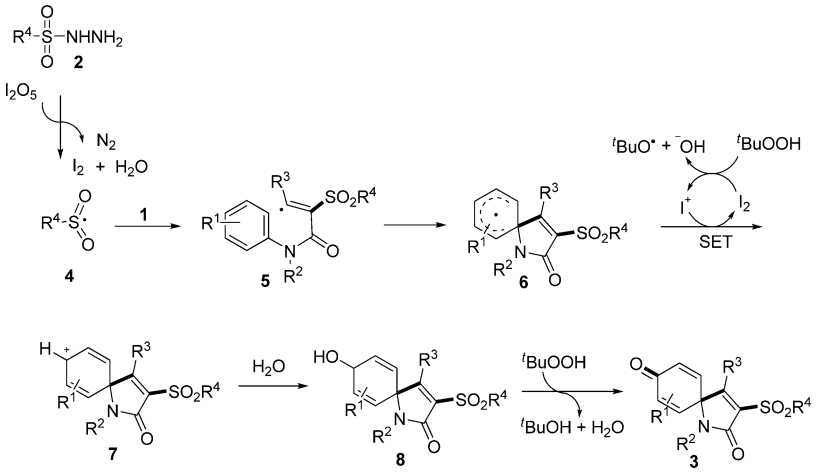
Scheme 4. Postulated Reaction Pathway



HRMS (ESI) calcd for $C_{22}H_{16}BrNO_4NaS$ $(M + Na)^+$ 491.9881, found 491.9885.

*1-Methyl-4-phenyl-3-(4-(trifluoromethyl)phenylsulfonyl)-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione (**3f**).* Compounds **3f** were obtained in 80% yield (91.8 mg) according to the general procedure (30 h); white solid; mp 252.3−254.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 8.2 Hz, 2H), 7.83 (d, J = 8.3 Hz, 2H), 7.49 (t, J = 7.5 Hz, 1H), 7.41 (t, J = 7.5 Hz, 2H), 7.18 (d, J = 7.1 Hz, 2H), 6.47 (d, J = 1.2 Hz, 4H), 2.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.9, 163.3, 163.2, 141.8, 135.9, 134.6, 130.7, 129.9, 128.2, 128.1, 127.8, 126.2 (q, J = 3.7 Hz), 68.5, 26.4; HRMS (ESI) calcd for $C_{23}H_{16}F_3NO_4NaS$ $(M + Na)^+$ 482.0650, found 482.0653.

*1-Methyl-3-(phenylsulfonyl)-4-p-tolyl-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione (**3g**).* Compounds **3g** were obtained in 76% yield (77 mg) according to the general procedure (20h); yellow solid; mp 184.5−186.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 7.3 Hz, 2H), 7.67 (t, J = 7.4 Hz, 1H), 7.56 (t, J = 7.7 Hz, 2H), 7.19 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 8.1 Hz, 2H), 6.45 (s, 4H), 2.83 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.2, 163.6, 162.5, 142.5, 140.8, 139.3, 136.2, 134.3, 134.3, 129.2, 129.1, 128.8, 127.8, 125.6, 68.3, 26.3, 21.5; HRMS (ESI) calcd for $C_{23}H_{19}NO_4NaS$ $(M + Na)^+$ 428.0932, found 428.0935.

*4-(4-Methoxyphenyl)-1-methyl-3-(phenylsulfonyl)-1-azaspiro-[4.5]deca-3,6,9-triene-2,8-dione (**3h**).* Compound **3h** was obtained in 75% yield (82.1 mg) according to the general procedure (22 h); yellow solid; mp 198.8−201.1 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.07 (d, J = 7.3, 2H), 7.67 (t, J = 7.4 Hz, 1H), 7.56 (t, J = 8.0 Hz, 2H), 7.21 (t, J = 8.8 Hz, 2H), 6.89 (d, J = 8.8 Hz, 2H), 6.49−6.43 (m, 4H), 3.83 (s, 3H), 2.81 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 183.3, 163.7, 162.1, 161.4, 142.7, 139.3, 135.6, 134.3, 134.2, 129.8, 129.2, 129.0, 120.6, 113.6, 68.2, 55.3, 26.2; HRMS (ESI) calcd for $C_{23}H_{19}NO_5NaS$ $(M + Na)^+$ 444.0882, found 444.0883.

*4-(4-Fluorophenyl)-1-methyl-3-(phenylsulfonyl)-1-azaspiro[4.5]-deca-3,6,9-triene-2,8-dione (**3i**).* Compound **3i** was obtained in 66% yield (67.5 mg) according to the general procedure (20 h); yellow solid; mp 186.6−190.1 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.06 (d, J = 7.2 Hz, 2H), 7.69 (t, J = 7.4 Hz, 1H), 7.58 (t, J = 7.8 Hz, 2H), 7.22−7.18 (m, 2H), 7.10 (t, J = 8.4 Hz, 2H), 6.50−6.44 (m, 4H), 2.85 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 182.9, 165.1, 162.6, 162.1 (d, J = 238.9 Hz), 142.1, 139.0, 137.1, 134.5, 130.1 (d, J = 8.6 Hz), 129.2, 129.1, 124.4 (d, J = 3.6 Hz),, 115.5 (d, J = 22.0 Hz), 68.3, 26.4; HRMS (ESI) calcd for $C_{22}H_{16}FNO_4S$ $(M + Na)^+$ 432.0682, found 432.0681.

*4-(4-Chlorophenyl)-1-methyl-3-(phenylsulfonyl)-1-azaspiro[4.5]-deca-3,6,9-triene-2,8-dione (**3j**).* Compound **3j** was obtained in 78% yield (82.9 mg) according to the general procedure (20 h); yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.04 (d, J = 7.4 Hz, 2H), 7.68 (t, J = 7.4 Hz, 1H), 7.56 (t, J = 7.8 Hz, 2H), 7.36 (d, J = 8.5 Hz, 2H), 7.12 (d, J = 8.5 Hz, 2H), 6.46 (s, 4H), 2.83 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 182.9, 163.2, 160.7, 142.1, 138.9, 137.2, 136.2, 134.5, 129.3, 129.2, 128.4, 126.9, 68.2, 26.4; HRMS (ESI) calcd for $C_{22}H_{16}ClNO_4NaS$ $(M + Na)^+$ 448.0386, found 448.0384.

*4-(4-Bromophenyl)-1-methyl-3-(phenylsulfonyl)-1-azaspiro[4.5]-deca-3,6,9-triene-2,8-dione (**3k**).* Compound **3k** was obtained in 80% yield (93.8 mg) according to the general procedure (20 h); yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.04 (d, J = 7.5 Hz, 2H), 7.69 (t, J = 7.4 Hz, 1H), 7.57 (t, J = 7.8 Hz, 2H), 7.53 (d, J = 8.4 Hz, 2H), 7.06 (d, J = 8.5 Hz, 2H), 6.49−6.43 (m, 4H), 2.84 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 182.9, 163.3, 160.7, 142.0, 138.9, 137.2, 134.6, 131.4, 129.4, 129.2, 129.2, 127.4, 125.2, 68.2, 26.4; HRMS (ESI) calcd for $C_{22}H_{17}BrNO_4S$ $(M + H)^+$ 468.9981, found 468.9983.

*1,4-Dimethyl-3-(phenylsulfonyl)-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione (**3l**).* Compounds **3l** were obtained in 60% yield (49.2 mg) according to the general procedure (20 h); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 7.2 Hz, 2H), 7.70 (t, J = 7.4 Hz, 1H), 7.59 (t, J = 8.0 Hz, 2H), 6.63 (d, J = 10.1 Hz, 2H), 6.32 (d, J = 10.1 Hz, 2H), 2.79 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.3, 163.8, 161.9, 143.3, 139.3, 135.4, 134.5, 134.4, 129.1, 128.9, 68.3, 26.3, 12.1; HRMS (ESI) calcd for $C_{17}H_{15}NO_4NaS$ $(M + Na)^+$ 352.0619 found 352.0623.

*1,6-Dimethyl-4-phenyl-3-(phenylsulfonyl)-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione (**3o**).* Compound **3o** was obtained in 81% yield (82 mg) according to the general procedure (24 h); white solid; mp 201.2−202.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 7.6 Hz, 2H), 7.68 (t, J = 7.4 Hz, 1H), 7.56 (t, J = 7.7 Hz, 2H), 7.47 (t, J = 7.4 Hz, 1H), 7.39 (t, J = 7.5 Hz, 2H), 7.18 (d, J = 7.4 Hz, 2H), 6.47−6.39 (m, 2H), 6.33 (s, 1H), 2.75 (s, 3H), 1.74 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.8, 163.9, 162.3, 150.6, 142.3, 139.3, 137.1, 134.4, 133.9, 133.0, 130.8, 129.1, 129.1, 128.3, 128.1, 127.8, 70.6, 26.0, 17.7; HRMS (ESI) calcd for $C_{23}H_{19}NO_4NaS$ $(M + Na)^+$ 428.0932, found 428.0934.

*6-Ethyl-1-methyl-4-phenyl-3-(phenylsulfonyl)-1-azaspiro[4.5]-deca-3,6,9-triene-2,8-dione (**3p**).* Compound **3p** was obtained in 83% yield (87 mg) according to the general procedure (20 h); yellow solid; mp 152.8−156.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 7.3 Hz, 2H), 7.68 (t, J = 7.4 Hz, 1H), 7.56 (t, J = 7.7 Hz, 2H), 7.46 (t, J = 7.5 Hz, 1H), 7.38 (t, J = 7.5 Hz, 2H), 7.14 (d, J = 7.2 Hz, 2H), 6.46 (dd, J_1= 1.5, J_2 = 9.9 Hz, 1H), 6.38 (d, J = 9.9 Hz, 1H), 6.34 (d, J = 1.6 Hz, 1H), 2.73 (s, 3H), 1.95 (dq, J_1 = 1.4, J_2 = 7.2 Hz, 2H), 1.11 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.0, 164.1, 162.8, 155.9, 142.6, 139.2, 137.0, 134.4, 133.8, 130.8, 130.3, 129.1, 128.3, 128.1, 127.8, 70.8, 26.2, 22.7, 10.2. HRMS (ESI) calcd for $C_{24}H_{21}NO_4NaS$ $(M + Na)^+$ 442.1089, found 442.1088.

*6-Fluoro-1-methyl-4-phenyl-3-(phenylsulfonyl)-1-azaspiro[4.5]-deca-3,6,9-triene-2,8-dione (**3q**).* Compound **3q** was obtained in 78% yield (79.7 mg) according to the general procedure (20 h); yellow solid; mp 204.1−205.6 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.03 (d, J = 7.5 Hz, 2H), 7.68 (t, J = 7.4 Hz, 1H), 7.56 (t, J = 7.7 Hz, 2H), 7.48 (t, J = 7.4 Hz, 1H), 7.42 (t, J = 7.4 Hz, 2H), 7.18 (d, J = 7.3 Hz, 2H), 6.44−6.36 (m, 2H), 6.16 (d, J = 12.6 Hz, 1H), 2.84 (s, 3H); ^{13}C

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NMR ($CDCl_3$, 100 MHz, ppm): δ 185.0 (d, J = 14.7 Hz), 167.2 (d, J = 288.2 Hz), 163.8, 159.9, 138.9, 138.6 (d, J = 3.0 Hz), 137.8, 134.5, 133.5, 130.7, 129.2, 129.1, 128.3, 127.8, 127.6, 114.7 (d, J = 8.4 Hz), 69.0 (d, J = 23.2 Hz), 26.2; HRMS (ESI) calcd for $C_{22}H_{16}FNO_4NaS$ $(M + Na)^+$ 432.0682, found 432.0680.

*6-Chloro-1-methyl-4-phenyl-3-(phenylsulfonyl)-1-azaspiro[4.5]-deca-3,6,9-triene-2,8-dione (**3r**).* Compound **3r** was obtained in 73% yield (77.5 mg) according to the general procedure (24 h); yellow solid; mp 196.6−198.4 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.04 (d, J = 7.5 Hz, 2H), 7.68 (t, J = 7.4 Hz, 1H), 7.57 (t, J = 7.8 Hz, 2H), 7.49 (t, J = 7.4 Hz, 1H), 7.41 (t, J = 7.5 Hz, 2H), 7.21 (d, J = 7.2 Hz, 2H), 6.65 (d, J = 1.4 Hz, 1H), 6.55 (d, J = 9.9 Hz, 1H), 6.48 (dd, J_1 = 1.4 Hz, J_2 = 9.9 Hz, 1H), 2.80 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 182.1, 163.8, 160.6, 148.4, 141.6, 139.1, 138.0, 134.4, 133.8, 133.4, 130.8, 129.1, 129.0, 128.2, 127.7, 71.4, 26.0; HRMS (ESI) calcd for $C_{22}H_{16}ClNO_4NaS$ $(M + Na)^+$ 448.0386, found 448.0390.

*6-Bromo-1-methyl-4-phenyl-3-(phenylsulfonyl)-1-azaspiro[4.5]-deca-3,6,9-triene-2,8-dione (**3s**).* Compound **3s** was obtained in 75% yield (87.9 mg)according to the general procedure (24 h); yellow solid; mp 208.9−211.3 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 8.04 (d, J = 7.5 Hz, 2H), 7.67 (t, J = 7.4 Hz, 1H), 7.56 (t, J = 7.7 Hz, 2H), 7.49 (t, J = 7.3 Hz, 1H), 7.41 (t, J = 7.5 Hz, 2H), 7.24 (d, J = 7.3 Hz, 2H), 6.89 (d, J = 1.0 Hz, 1H), 6.65 (d, J = 9.9 Hz, 1H), 6.50 (dd, J_1 = 1.0 Hz, J_2 = 9.9 Hz, 1H), 2.80 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 181.4, 163.7, 160.8, 142.0, 141.2, 139.1, 137.9, 134.4, 133.2, 130.8, 129.1, 128.2, 127.8, 127.7, 71.8, 26.0; HRMS (ESI) calcd for $C_{22}H_{16}BrNO_4NaS$ $(M + Na)^+$ 491.9881, found 491.9884.

*6-Iodo-1-methyl-4-phenyl-3-(phenylsulfonyl)-1-azaspiro[4.5]-deca-3,6,9-triene-2,8-dione (**3t**).* Compound **3t** was obtained in 76% yield (98.1 mg) according to the general procedure (24 h); yellow solid; mp 215.5−219.3 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 8.05 (d, J = 7.5 Hz, 2H), 7.66 (t, J = 7.4 Hz, 1H), 7.55 (t, J = 7.7 Hz, 2H), 7.48 (t, J = 7.4 Hz, 1H), 7.40 (t, J = 7.5 Hz, 2H), 7.26 (d, J = 7.3 Hz, 2H), 7.21 (d, J = 1.2 Hz, 1H), 6.76 (d, J = 9.9 Hz, 1H), 6.53 (dd, J_1 = 1.2 Hz, J_2 = 9.9 Hz, 1H), 2.78 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 180.3, 163.6, 161.3, 145.8, 141.6, 139.0, 137.9, 134.4, 133.3, 130.8, 129.1, 129.1, 128.1, 128.0, 127.6, 121.6, 72.4, 26.1; HRMS (ESI) calcd for $C_{22}H_{16}INO_4NaS$ $(M + Na)^+$ 539.9742, found 539.9743.

*1,7,9-Trimethyl-4-phenyl-3-(phenylsulfonyl)-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione (**3u**).* Compound **3u** was obtained in 89% yield (93.2 mg) according to the general procedure (24 h); yellow solid; mp 207.2−210.5 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 8.04 (d, J = 7.9 Hz, 2H), 7.66 (t, J = 7.4 Hz, 1H), 7.55 (t, J = 7.7 Hz, 2H), 7.41 (t, J = 7.3 Hz, 1H), 7.35 (t, J = 7.4 Hz, 2H), 7.07 (d, J = 7.4 Hz, 2H), 6.19 (s, 2H), 2.81 (s, 3H), 1.86 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 184.7, 163.5, 163.5, 141.6, 139.4, 136.7, 135.9, 134.3, 130.0, 129.1, 129.1, 128.8, 127.7, 127.7, 68.9, 26.4, 16.1. HRMS (ESI) calcd for $C_{24}H_{21}NO_4NaS$ $(M + Na)^+$ 442.1089, found 442.1082.

*1,7-Dimethyl-4-phenyl-3-(phenylsulfonyl)-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione (**3v**).* Compound **3v** was obtained in 75% yield (76 mg) according to the general procedure (24 h); yellow solid; mp 230.3−233.8 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 8.06 (d, J = 7.5 Hz, 2H), 7.68 (t, J = 7.4 Hz, 1H), 7.57 (t, J = 7.8 Hz, 2H), 7.45 (t, J = 7.4 Hz, 1H), 7.39 (t, J = 7.4 Hz, 2H), 7.13 (d, J = 7.2 Hz, 2H), 6.42 (s, J = 1.2 Hz, 2H), 6.22 (d, J = 1.2 Hz, 1H), 2.83 (s, 3H), 1.90 (s, 3H); ^{13}CNMR ($CDCl_3$, 100 MHz, ppm) δ 183.9, 163.5, 162.7, 142.1, 142.0 140.7, 139.3, 136.9, 134.3, 134.1, 129.2, 129.1, 127.9, 127.9, 127.8, 68.9, 26.4, 15.9; HRMS (ESI) calcd for $C_{23}H_{19}NO_4NaS$ $(M + Na)^+$ 428.0932, found 428.0933.

*7-Chloro-1-methyl-4-phenyl-3-(phenylsulfonyl)-1-azaspiro[4.5]-deca-3,6,9-triene-2,8-dione (**3w**).* Compound **3w** was obtained in 63% yield (66.9 mg) according to the general procedure (24h); yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 8.05 (d, J = 7.4 Hz, 2H), 7.68 (t, J = 7.4 Hz, 1H), 7.57 (t, J = 7.8 Hz, 2H), 7.47 (t, J = 7.4 Hz, 1H), 7.41 (t, J = 7.4 Hz, 2H), 7.14 (d, J = 7.1 Hz, 2H), 6.69 (s, 1H), 6.52 (d, J = 1.2 Hz, 2H), 2.88 (s, 3H); ^{13}CNMR ($CDCl_3$, 100 MHz, ppm) δ 176.4, 163.2, 161.3, 142.9, 139.0, 138.0, 137.7, 136.9, 134.5, 133.3, 130.6, 129.2, 129.1, 128.2, 128.1, 127.8, 70.0, 26.6; HRMS (ESI) calcd for $C_{22}H_{16}ClNO_4NaS$ $(M + Na)^+$ 448.0386, found 448.0389.

*7-Bromo-1-methyl-4-phenyl-3-(phenylsulfonyl)-1-azaspiro[4.5]-deca-3,6,9-triene-2,8-dione (**3x**).* Compound **3x** was obtained in 68% yield (79.7 mg) according to the general procedure (24 h); orange oil; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 8.05 (d, J = 7.4 Hz, 2H), 7.69 (t, J = 7.4 Hz, 1H), 7.57 (t, J = 7.8 Hz, 2H), 7.48 (t, J = 7.4 Hz, 1H), 7.42 (t, J = 7.4 Hz, 2H), 7.14 (d, J = 7.1 Hz, 2H), 6.96 (s, 1H), 6.53 (d, J = 1.0 Hz, 2H), 2.89 (s, 3H); ^{13}CNMR ($CDCl_3$, 100 MHz, ppm) δ 176.2, 163.3, 161.0, 142.9, 142.3, 139.0, 136.9, 134.5, 132.7, 130.6, 129.5, 129.3, 129.1, 128.1, 128.1, 127.8, 70.7, 26.7; HRMS (ESI) calcd for $C_{22}H_{16}BrNO_4NaS$ $(M + Na)^+$ 491.9881, found 491.9884.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The X-ray crystallographic data of **3a**, the copies of ^{1}H NMR and ^{13}C NMR spectra for all compounds. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00361.

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Notes

The authors declare no competing financial interest.

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