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Unexpected Substituent Effects in Spiro-Compound Formation: Steering *N*-Aryl Propynamides and DMSO toward Site-Specific Sulfination in Quinolin-2-ones or Spiro[4,5]trienones

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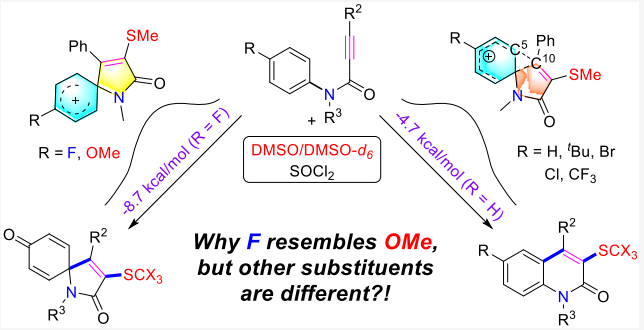
ABSTRACT: A highly substituent-dependent rearrangement allows for the novel and $SOCl_2$-induced divergent synthesis of 3-methylthioquinolin-2-ones and 3-methylthiospiro[4.5]trienones through intramolecular electrophilic cyclization of *N*-aryl propynamides. DMSO acts as both solvent and sulfur source, and use of DMSO-h_6/d_6 enables the incorporation of SCH_3 or SCD_3 moieties to the 3-position of the heterocyclic framework. Different *para*-substituents trigger divergent reaction pathways leading to the formation of quinolin-2-ones for mild substituents and spiro[4,5]-trienones for both electron-withdrawing and -donating substituents, respectively. On the basis of both computational and experimental results, a new mechanism has been put forward that accounts for the exclusive spirolization/defluorination process and the surprising substituent effects.



INTRODUCTION

Quinolinones and spiro[4.5]trienones both have been recognized as important heterocyclic skeletons of biologically active molecules.[1] They have been reported to possess diverse pharmacological properties such as anticancer,[2] anti-HCV,[3] anti-inflammatory,[4] and antidiabetic activities.[5] Also, these heterocyclic frameworks can be found in a plethora of biologically active natural compounds.[6] In parallel, sulfides are a class of important compounds, many of which have been found to exhibit unique pharmacological activities.[7] Most importantly, they have also served as the key building blocks in many organic transformations,[8] and the introduction of sulfenyl groups into drug molecules may significantly enhance their biological activities.[9] As a result, it is of significant interest to develop methods to introduce a sulfenyl group into the quinolinone or spiro[4.5]trienone skeletons.

Some protocols utilizing metal catalysts have been applied to construct the sulfenylated quinolinone and spiro[4.5]trienone skeletons.[10] For example, Gao and co-workers developed an $AlCl_3$-catalyzed intramolecular cyclization of *N*-arylpropynamides to yield 3-sulfenyl quinolinones and spiro[4.5]trienones, using *N*-sulfanylsuccinimides as the sulfur donor (Scheme 1a).[10c] A similar strategy for synthesizing 3-thioazaspiro[4,5]-trienones from thiophenols was developed through silver-catalyzed radical oxidative spirocyclization.[10d] Analogously, Li and co-workers realized the synthesis of 3-sulfenyl azaspiro-[4,5]trienones via a Cu-catalyzed *ipso*-cyclization of *N*-(paramethoxyaryl) propynamides with disulfides (Scheme 1b).[10e]

For environmental reasons, more recently there is a drive toward metal-free synthetic methods to construct these two classes of heterocycles.[11] For example, Wu and colleagues reported an iodine-catalyzed electrophilic cyclization approach by using sodium arylsulfinates as sulfur source, which furnishes 3-sulfenylquinolinone derivatives (Scheme 1c).[11a] In 2019, Guo and co-workers realized an electrochemical oxidative cyclization of alkynamides, furnishing quinolinones substituted with chalcogen substituent (Scheme 1d).[11b] Evidently these developments combine an increasing ease of use with environmentally friendlier approaches. Yet, in all the above transformations, the sulfur source was still a custom chemical, which required additional synthesis, such as RSO_2Na, a sulfonyl succinimide, or a disulfide. To overcome this issue, and further reduce the complexity of the reaction, in this communication we report, first, that readily available DMSO and DMSO-d_6 could be used as sulfur source, and $SOCl_2$ as activating agent, to enable the intramolecular cyclization of *N*-

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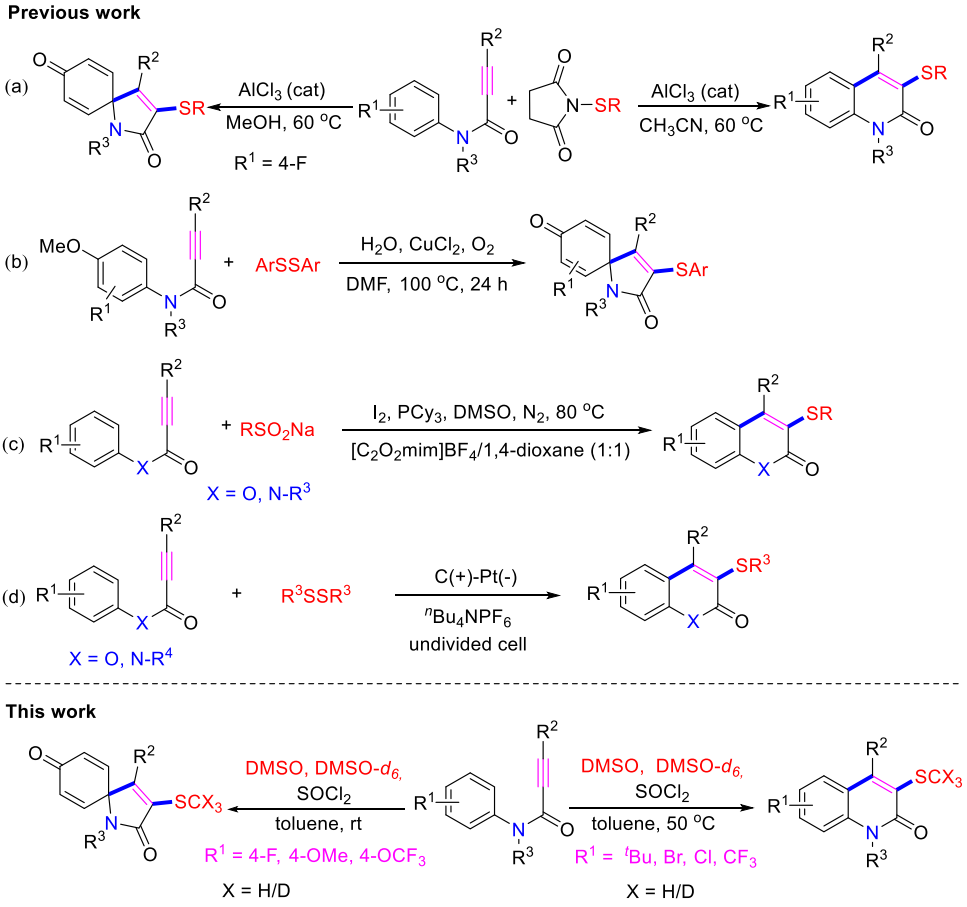
Scheme 1. Strategies for the Synthesis of 3-Sulfenylated Quinolin-2-ones and Azaspiro[4,5]trienones



aryl propynamides, leading to an efficient construction of 3-methylthioquinolin-2-one and 3-methylthiospiro[4.5]trienone skeletons.

DMSO, possessing the advantages of being inexpensive, stable, and low-toxicity, and allowing for easy handling, has been widely used not only as a polar organic solvent, but also as an oxidant or building block in various organic transformations.[12] For example, DMSO has found application in the Swern oxidation,[13] Pfitzner-Moffatt oxidation,[14] Albright-Goldman oxidation,[15] Parikh-Doering oxidation,[16] and other newly reported methods.[17] Most strikingly, DMSO can also be employed as the source of $-CH_2SMe$, $-SO_2Me$, or $-SMe$, to afford thio-modified structures.[18] However, a literature survey indicated that the application of DMSO as a sulfur source to introducing $-SMe$ group has remained somewhat underexplored.[19] In line with our interest in developing methods for the construction of S-containing heterocycles by using DMSO as sulfur source,[20] we report here the reaction of *N*-aryl propynamides with DMSO/DMSO-d_6 and $SOCl_2$, for synthesis of 3-methylthioquinolin-2-ones and 3-methylthiospiro[4.5]trienones. DMSO-d_6 can also take the place of DMSO, thereby providing access to the corresponding deuterated counterparts, which might be useful for further biological studies as deuterated drugs[21] or analytical reference compounds.

Second, we noticed remarkable substituent effects. Typically, reactivity trends over electronic substituents vary such that there is a somewhat continuous line with monotonous behavior from electron-withdrawing substituents via electronically neutral ones to electron-donating ones.[22] Here, however, we describe that for a wide range of electronically "neutral" substituents a specific reaction path is followed, while for both specific electron-withdrawing substituents and electron-donating ones the reaction is steered into another direction. Via a detailed quantum chemical analysis, it is shown how both these routes occur, and thereby form the basis of two rather different, but both high-yielding synthetic routes.

RESULTS AND DISCUSSION

With reference to the reactions in our previous work,[20] we initiated our studies by treating *N*-methyl-*N*,3-diphenylpropiolamide **1a** (0.5 mmol) with DMSO (1 mL) and $SOCl_2$(1.0 mmol) at 25 °C for 12 h. We were pleased to note that the desired 1-methyl-3-(methylthio)-4-phenylquinolin-2(1*H*)-one **2a** was obtained in 22% yield (Table 1, entry 1). When the dosage of $SOCl_2$ was increased, the yield of **2a** improved significantly and the time needed was shortened (Table 1, entries 2−3). However, when the dosage of $SOCl_2$ was increased to 3.0 equiv, the yield was not obviously enhanced (Table 1, entry 4). We also carried out the reaction at higher temperature, and found that the reaction time could be greatly shortened, albeit the yield was not improved (Table 1, entries 5−6). Further studies showed that other additives—including TFAA, *p*-TsCl and oxalyl chloride—were not superior to $SOCl_2$ (Table 1, entries 7−10). Solvents screening was carried out and the results indicated that toluene, compared with EtOAc, MeCN, 1,4-dioxane, THF, and DCE, is the most appropriate cosolvent for this conversion (Table 1, entries 11−

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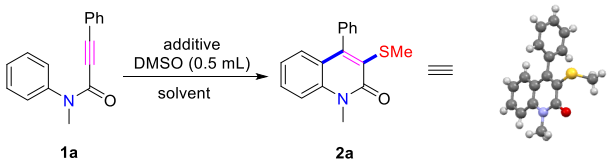
Table 1. Optimization of Reaction Conditions[a]



1a 2a

entry	solvent	additive (equiv)	T (°C)	time (h)	yield (%)[b]
1	DMSO	$SOCl_2$ (1.0)	rt	12	22
2	DMSO	$SOCl_2$ (1.5)	rt	12	35
3	DMSO	$SOCl_2$ (2.0)	rt	3	68
4	DMSO	$SOCl_2$ (3.0)	rt	3	73
5	DMSO	$SOCl_2$ (2.0)	50	0.5	76
6	DMSO	$SOCl_2$ (2.0)	70	0.5	78
7	DMSO	$(COCl)_2$ (2.0)	50	8	56
8	DMSO	$(COCl)_2$ (3.0)	50	8	62
9	DMSO	TFAA (2.0)	50	12	NR
10	DMSO	TsCl (2.0)	50	12	NR
11	EtOAc	$SOCl_2$ (2.0)	50	0.5	20
12	MeCN	$SOCl_2$ (2.0)	50	0.5	63
13	**toluene**	**$SOCl_2$ (2.0)**	**50**	**0.5**	**84**
14	dioxane	$SOCl_2$ (2.0)	50	0.5	45

[a]Reaction conditions: **1a** (0.5 mmol), DMSO (0.5 mL) in solvent (0.5 mL), unless otherwise stated. [b]Isolated yield.

14). After variation over a series of experimental parameters, the best conditions were determined to be 0.5 mmol of **1a** with 2.0 equiv of $SOCl_2$ and 0.5 mL of DMSO in 0.5 mL of toluene at 50 °C.

Under these optimized conditions, the scope of this newly established thiocyclization method was investigated, and the results are depicted in Table 2. It was found that when R^1 is an alkyl group, the reaction proceeded well to give the corresponding 3-(methylthio)quinolin-2-ones in good yield (Table 2, **2b−d**). For the substrates bearing a Cl, Br, naphthyl, or CF_3 group, the reaction gave the corresponding product in relatively lower yield (Table 2, **2e−i**). When the R^2 group is a phenyl ring bearing electron-donating or electron-withdrawing groups, the reaction proceeded smoothly to deliver the corresponding target products **2j−o** in satisfactory yield. It is worth noting that this method is not exclusive to internal alkynes, but also suitable for substrates with an terminal alkyne moiety, as the corresponding substrate can effectively afford the desired compound **2p** in moderate yield. Furthermore, the methyl group on the N atom in amide substrates can also be replaced with ethyl, isopropyl, and phenyl substituent, with the *N*-substituted 3-methylthioquinolin-2-one products **2q−s** again obtained in satisfactory yield. It was also found that when dihydroquinolinamide **1t** was subjected to the standard conditions, the thioheterocyclic compound **2t** can be achieved. Finally, DMSO can also be replaced by DMSO-d_6, and the deuterated 3-methylthioquinolin-2-one **2u** can be obtained in equally good yield by using this method. In addition, we explored a gram-scale experiment by subjecting 1 g of substrate **1a** to the standard conditions. We were pleased to find that the reaction occurred smoothly to form **2a** in 80% yield.

A further widening of the range of investigated electronic substituents yielded a remarkable substituent effect: upon substitution of the aniline with a fluorine, methoxy, or trifluoro methoxy group at the *para* position of the aniline moiety the reaction takes a different course. During our investigations, it became clear we could use this systematically to our advantage, as with such substrates this alternative pathway was efficiently followed to give 3-(methylthio) spiro[4,5]trienone **3a**.

To investigate the scope and usefulness of these findings, a series of *N*-aryl propynamides with *para*-fluoro or *para*-methoxy moiety was prepared and subjected to the standard conditions. Invariably, the corresponding spiro-products could be obtained with high yield within 20 min (Table 3, **3b−f**). Unfortunately, the method is not applicable to the substrates bearing no phenyl group on the terminal alkyne moiety. When substrates with R^2 being H and R being OMe or F were applied, the corresponding products could not be obtained (not shown). When such substrates also displayed an additional R^1 substituent in the *ortho* or *meta* position of the aniline moiety, then still the reaction afforded the desired products in a moderate to good yield (Table 3, **3g−j**). Interestingly, we observed that the *ortho*-fluoro substituted *N*-aryl propynamide can also be converted to spiro[4,5]trienone **3k**. Finally, and in analogy to the 3-methylthioquinolin-2-one before, DMSO can be replaced with DMSO-d_6, to enable the synthesis of deuterated spiro[4,5]trienones (Table 3, **3l**).

With regard to the spirolization of the F-substituted substrates, we and others postulated a concerted pathway containing simultaneous nucleophilic attack and spiro-formation processes (Scheme 2).[10c,23] As this overall pathway would depend on significant positive charge development on the F-bound *ipso*-carbon atom to make attack by, e.g., methanol (Scheme 2a) or triflate attractive (Scheme 2b), and also would require a large reduction of entropy in the transition state to allow for the synchronous intermolecular nucleophilic attack and the intramolecular ring closure, we wondered whether a conceptually simpler alternative might be found.

On the basis of our experimental results, previous reports,[10c,d,20,23,24] and wB97XD/6-311+G(d,p) calculations,[25] we propose substituent-dependent mechanistic pathways for the construction of 3-methylthioquinolin-2-one and 3-methylthiospiro[4.5]trienone skeletons, respectively (Scheme 3). We will discuss these in detail for three different substituents, R = *para*-H, *para*-F, and *para*-OMe, as they represent the various classes of substituents for which different reactivities have been observed. First, CH_3SCl **A** is generated in situ from the reaction of DMSO with $SOCl_2$ via the dimethylsulfochlorine cation intermediate through an interrupted Pummerer reaction process.[26] Then, the electrophilic addition of CH_3SCl **A** to the C≡C bond of **1a** furnished for all R groups the cyclic sulfonium cation intermediate **B**.[13,27]

This reaction was calculated to be slightly exothermic (ΔH = −4 to −5 kcal/mol) for all three substituents, and the resulting three-membered ring species more stable than the isomeric α-phenyl-substituted vinyl cations. Initially, given the demonstrated experimental relevance of highly strained (C═C—S) three-membered rings,[28] we hypothesized these could rearrange to cations **C**, since this would form a 6-membered ring and only maintain one formally sp^2-hybridized carbon atom in the three-membered ring. Such rearrangement could then by following by an exothermic opening of the three-membered ring, forming species **D**. From here on the mechanistic routes would then diverge, as for R = H this would lead to the bicyclic compound **2a**, while for R = F and R = OMe, spiroformation should occur. Such reasoning—indicated at the top of Scheme 2—was, however, barred when we studied these pathways quantum chemically. First it turned out that the **B** ∀ **C** conversion was endothermic by ≥20

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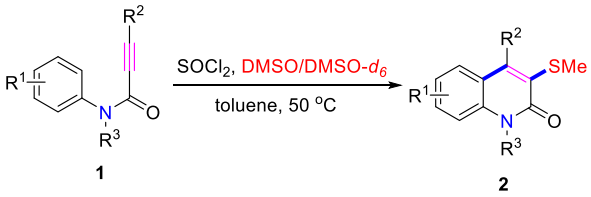
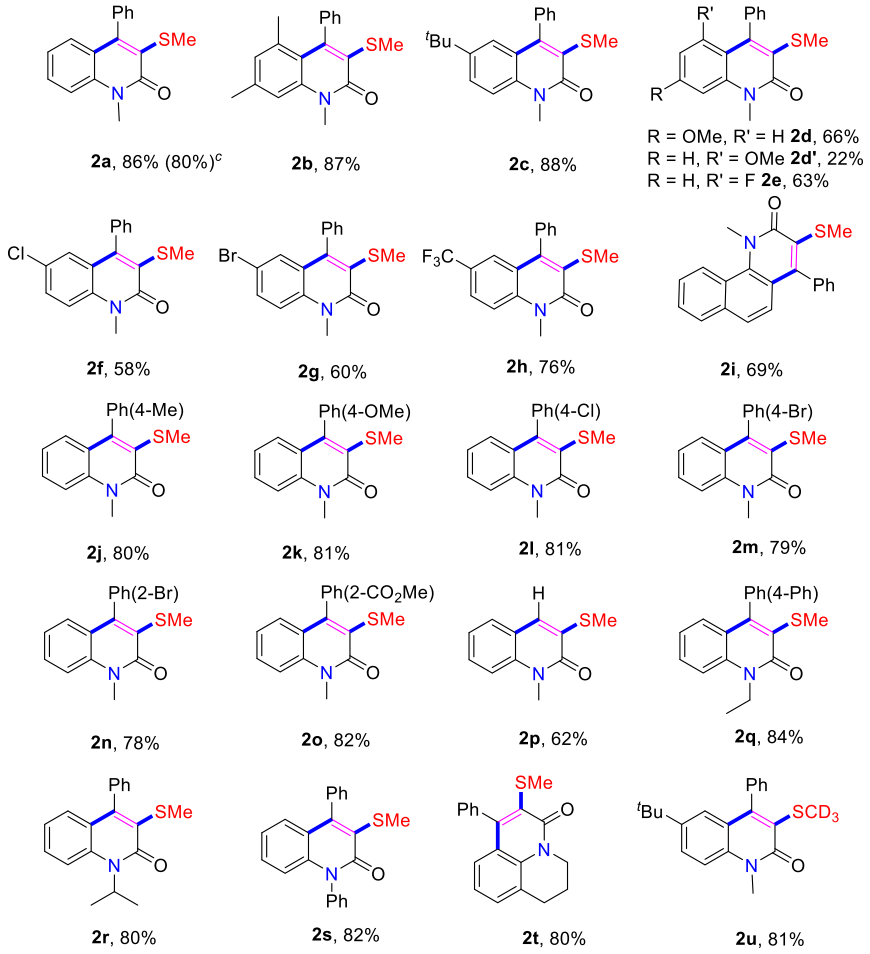
Table 2. $SOCl_2$ and DMSO/DMSO-d_6 Mediated Synthesis of 3-Methylthioquinolin-2-ones[a,b]



1 2



[a]Reaction conditions: **1** (0.5 mmol), $SOCl_2$ (1.0 mmol), DMSO or DMSO-d_6 (0.5 mL)/toluene (0.5 mL), 50 °C, 0.5 h. [b]Isolated yield. [c]Gram-scale experiment.

kcal/mol for all these three substituents, with enthalpic activation barriers of >25 kcal/mol. Such barrier heights for monomolecular rearrangements are not compatible with the above experimental observations of facile reaction at room temperature or 50 °C. Next, the cationic species **D** displayed a tendency for proton loss to any base (Cl^- or DMSO) without any activation barrier, and reaction enthalpies typically −40 kcal/mol for all three substituents. Since this is favorable for the formation of **2a**, it was hard to imagine how spiro-compounds **3a** could efficiently be obtained from here for R = F and OMe, which displayed an equally facile proton transfer. Finally, it turned out that the **D** ∀ **E** transition was actually uphill for R = H (16.9 kcal/mol) and R = F (10.4 kcal/mol), and only exothermic for R = OMe (−4.2 kcal/mol).

Since it thus seemed unlikely that **D** was an intermediate to **3a**, we investigated whether spiro-cations **E** could be formed directly from cations **B**, thereby making the spiro-cation the central intermediate in this pathway. This indeed turned out to correspond to a very facile reaction, with enthalpies of −6.0, −8.7, and −23.4 kcal/mol, for R = H, F, and OMe, respectively, and low activation barriers of 2.2 and 1.6 kcal/mol for R = H and F, respectively. Such low barrier implies that, in contrast to earlier suggestions, no nucleophilic assistance is needed or even likely for spiro-formation.[10c,23] While F is generally thought of as an electron-withdrawing substituent (e.g., σ_m and σ_p values of 0.34 and 0.06, respectively),[29] when bound directly to a (partially) positive carbon atom [C^+−F or $C^{\delta+}$−F] it is actually frequently stabilizing due to resonance effects,[30] in line with the stabilization observed here compared to R = H. For R = OMe intermediate **B** is a verified minimum (no imaginary vibrational frequencies), but no proper transition state could be located, and a relaxed potential energy scan suggests <0.5 kcal/mol as activation barrier.

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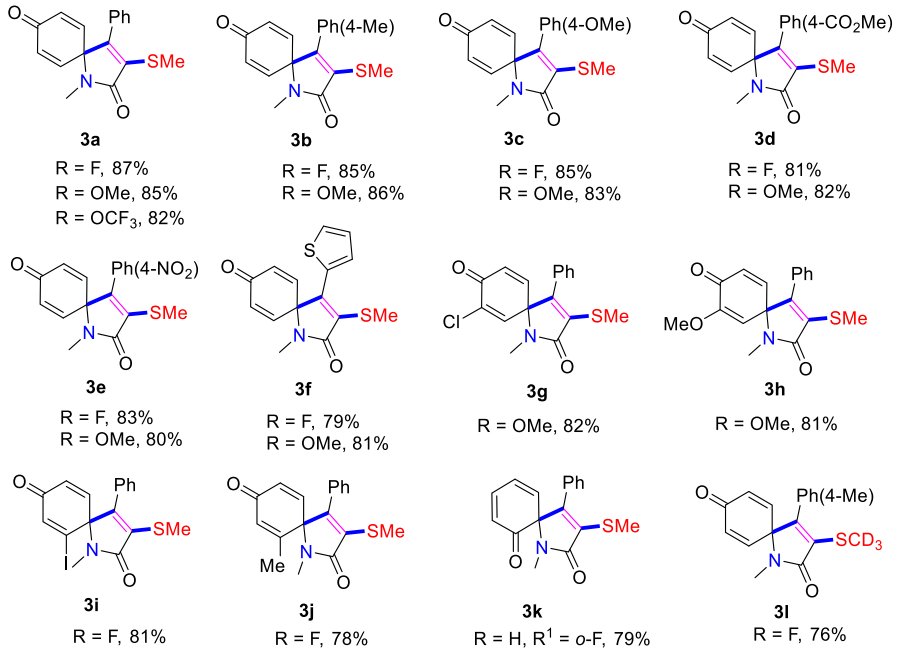
Table 3. $SOCl_2$ and DMSO/DMSO-d_6 Mediated Synthesis of 3-Methylthiospiro[4.5]trienones[a,b]

1' R = F, OMe, OCF_3 3



3a R = F, 87%; R = OMe, 85%; R = OCF_3, 82%

3b R = F, 85%; R = OMe, 86%

3c R = F, 85%; R = OMe, 83%

3d R = F, 81%; R = OMe, 82%

3e R = F, 83%; R = OMe, 80%

3f R = F, 79%; R = OMe, 81%

3g R = OMe, 82%

3h R = OMe, 81%

3i R = F, 81%

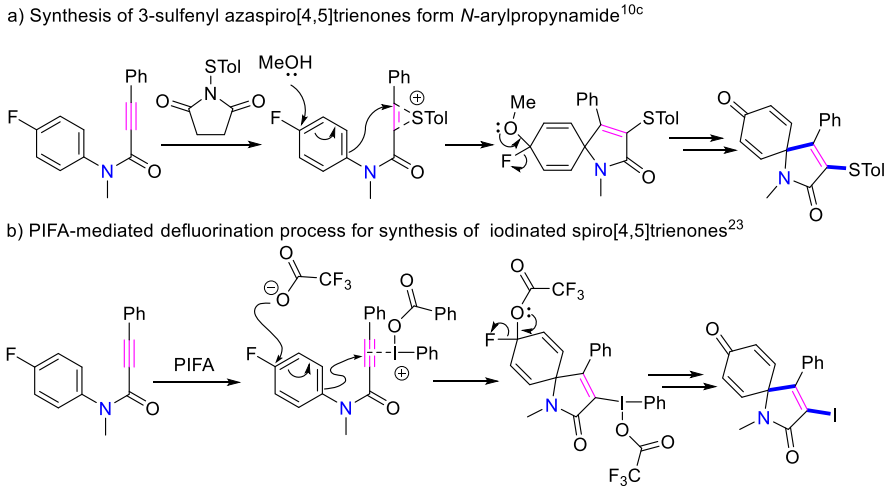
3j R = F, 78%

3k R = H, R^1 = *o*-F, 79%

3l R = F, 76%

[a]Reaction conditions: 1′ (0.5 mmol), $SOCl_2$ (1.0 mmol), DMSO or DMSO-d_6 (0.5 mL)/toluene (0.5 mL), rt, 20 min. [b]Isolated yield.

Scheme 2. Reported Mechanistic Pathways of Defluorination



The high stability of cation **E**-*OMe* basically shuts of any competing pathway. This cation then reacts effectively in an S_N2 methyl transfer to chloride anion (ΔH = −11.3 kcal/mol and $\Delta H^{\ddagger}$ = 13.5 kcal/mol). This barrier may, in reality, be a bit lower, as the real solvent is not DMSO (as consistently used in the calculations), but 50% DMSO/50% toluene, which likely reduces the solvation of chloride anion and thus increases its reactivity. Since the most likely alternative—methyl transfer on the S−CH_3 moiety—required a barrier precisely 20.0 kcal/mol higher than attack on the methoxy group, this explains the high-yielding synthesis of **3a** for R = OMe.

For the R = H and F, routes from **E** to **D** were investigated by gradually bringing carbon atoms C5 an C10 closer together. To our surprise, this yielded a cyclopropane cation **F**, as intermediate along the path to **D**. This rearrangement actually competes with attack by the DMSO oxygen atom on the

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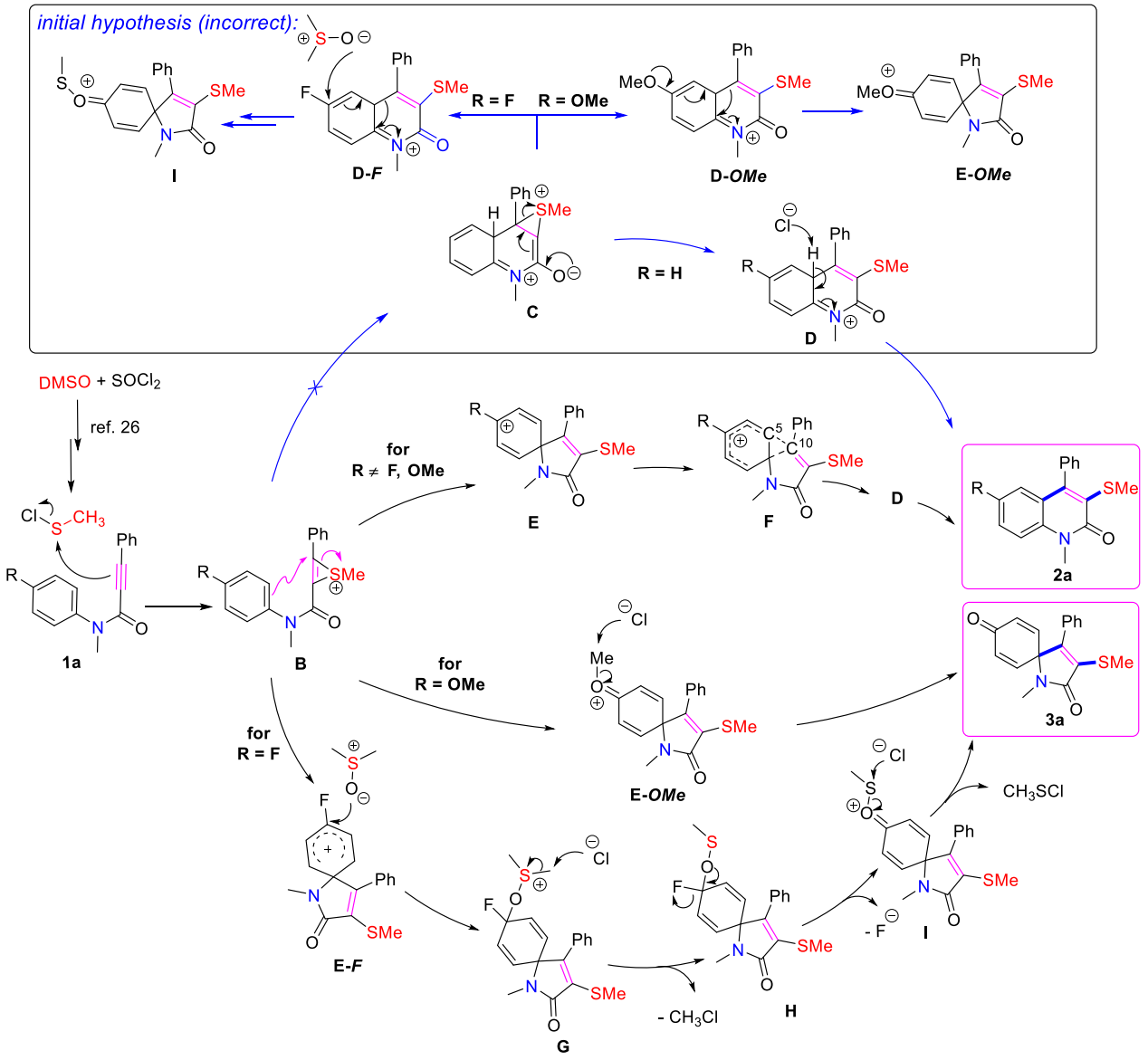
Scheme 3. Proposed Mechanistic Pathways: (Top) Initial, Incorrect Hypothesis; (Bottom) Detailed Routes Leading to Either 2a or 3a in Highly Substituent-Dependent Manners



formally positively charged *ipso*-C atom (as indicated for R = F, leading to intermediate **G**). For both R = H and R = F, the mechanistic dichotomy is less sharp than with R = OMe, as both routes occur with relatively small barriers, but they clearly point to the observed pathways. In one direction, the rearrangement to the cyclopropane cation **F** is uphill by 1.3 kcal/mol for R = H, and by 4.3 kcal/mol for R = F, with corresponding differences in the respective activation barriers. Subsequently, the reaction toward **D** is exothermic for both R = H and R = F, but less exothermic for R = F than for R = H (−14.2 vs −18.2 kcal/mol, with corresponding differences in the TS energies). As shown in Figure 1, the energy of this **TS-4** would be highest along the reaction pathway from **B** toward **D**. While the differences are small, both steps would yield more of **2a** for R = H than for R = F. In the other direction, the reaction of DMSO with spiro-cations **G** is exothermic for both R = H and for R = F (−12.6 and −14.2 kcal/mol, respectively, while it is endothermic by 1.3 kcal/mol for R = OMe), but the *ipso*-carbon atom displays a significantly larger positive (natural population) charge for R = F (+0.669) than for R = H (+0.092), which is thus more attractive for reaction with the partially negatively charged O atom on DMSO.

Interestingly, for other substituents, largely the bicyclic compound route toward **D** is formed, leading in that case to **2e**. As a point in case, it is worth noting that for substrate **1e** bearing a fluoro group at *meta*-position of anilide, the reaction adopted, like, e.g., *para*-H, the path to give 3-methylthioquinolin-2-one **2e**. For this *meta*-F compound the **B** ∀ **E** ∀ **F** ∀ **D** sequence was downhill for all three steps, with energy differences of −1.2, −2.9, and −20.3 kcal/mol, respectively. Most striking is that the transition from spiro-cation **E** to cyclopropane cation **F** is thus exothermic, while it was endothermic for, e.g., *para*-H and *para*-F. This indeed is in line with our hypothesis that the mechanistic bifurcation point only leads to capture by nucleophiles in particular cases.

Once via these respective paths intermediates **D** (R = H) or **E**-*F* (R = F) are formed, the pathways are fixed. As said, cation **D** (R = H) will undergo a facile and highly exothermic proton

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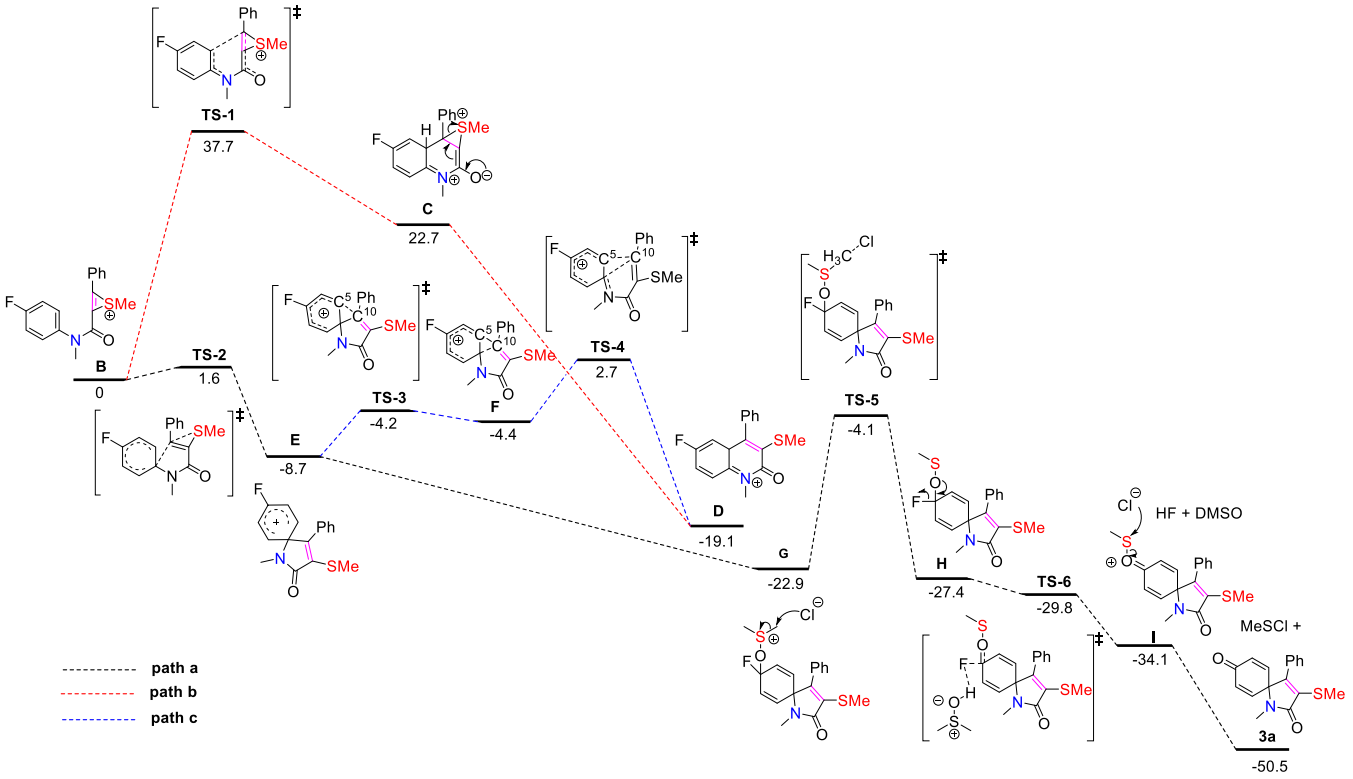


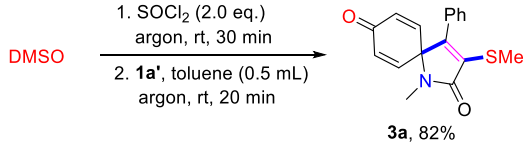
Figure 1. Free energy profile (kcal/mol) of the formation of intermediate **D** or 3-(methylthio) spiro[4,5]trienone **3a**.

loss to yield **2a**. For the DMSO-bound cation **G**, a multistep, yet consistently low-barrier route exists toward the oxidized spiro-compound **3a**. First, chloride anion can induce a methyl transfer S_N2 reaction ($\Delta H^{\ddagger}$ = 18.8 kcal/mol, but—as noted before—likely somewhat lower due to the 50/50 DMSO/toluene mixture rather than pure DMSO). As seen from Figure 1, this is the rate-limiting step in the formation of **3a**, and the overall preference to form **3a** rather than **D** and then **2a** is determined by the relative energies of **TS-4** and **TS-5**: for the *para*-F substituent **TS-5** is lower in energy by about 7 kcal/mol, thereby thus strongly favoring the route toward **3a**. The resulting neutral $C(-F)OSCH_3$ compound **H** can now easily lose F^- by the formation of HF. Assuming protonated DMSO as the proton source, this transfer proceeds with an activation barrier of only 6.8 kcal/mol. The resulting $[CH_3-S-O-C^+]$ species **I** then reacts highly exothermically and without an activation barrier with Cl^- under cleavage of the S−O bond. This reaction step thus reforms CH_3SCl and yields the oxidized spiro-product **3a**.

Finally, to experimentally confirm this mechanistic pathway at least partially, we aimed to elucidate the source of the carbonyl oxygen in the oxidized spiro-compound **3a**. To this aim we conducted the transformation of substrate **1a′** in an argon atmosphere. To our delight the corresponding product **3a** was still afforded in 82% yield (Scheme 4).

This result is indeed in line with the idea that DMSO is the oxygen source when the *para* position of aniline was substituted with a F atom. For substrates bearing a *para*-methoxy or *para*-trifluoromethoxy groups, the carbonyl oxygen in the final product **3a** might come from the OMe or OCF_3 groups substituted therein.[24]

Scheme 4. Control Experiment Confirming That DMSO Is the Oxygen Source



CONCLUSIONS

A metal-free and fast protocol was developed to synthesize 3-methylthioquinolin-2-ones and 3-methylthiospiro[4.5]-trienones via an electrophilic intramolecular cyclization of *N*-aryl propynamides that requires only DMSO and $SOCl_2$. This protocol provides the first route to introduce a SCH_3 or SCD_3 group into the biologically interesting quinolin-2-one and spiro[4.5]trienone skeletons. The synthetic outcome can be conveniently steered to or away from the spiro compounds, by making use of a remarkable substituent effect that was outlined in detail by quantum chemical methods, and thereby also shed light on a range of analogous but up to now poorly understood spiro-forming cyclization reactions.

EXPERIMENTAL SECTION

General Experimental Information. All reagents were purchased from commercial sources and were used without further purification. All solvents were purified and dried according to standard methods prior to use. *N*-Aryl propynamides **1** were prepared based on literature procedures.[23,31] ^1H and ^{13}C NMR spectra were recorded on 400 or 600 MHz spectrometer at 25 °C. Chemical shifts values are given in ppm and referred as the internal standard to TMS: 0.00 ppm. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). The coupling constants *J*, are reported in Hertz (Hz). High resolution mass spectrometry (HRMS) was obtained on a Q-TOF micro

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spectrometer. Melting points were determined with a micro-melting-point apparatus. TLC plates were visualized by exposure to ultraviolet light. Flash column chromatography was performed over silica gel (200−300 m) using a mixture of ethyl acetate (EtOAc) and petroleum ether (PE).

Experimental Procedures and Spectroscopic Data. *Preparation of Product 2 or 3.* The *N*-Arylpropynamide (0.5 mmol, 1.0 equiv) was added to a mixture of toluene (0.5 mL) and DMSO or DMSO-d_6 (0.5 mL) in a flask with stir bar, and then $SOCl_2$ (1.0 mmol, 2.0 equiv) was added dropwise at room temperature. Then the mixture was stirred at 50 °C (oil bath) or room temperature until the substrate was completely consumed. The mixture was cooled to room temperature and was treated with saturated aq. $NaHCO_3$ (30 mL). The mixture was extracted with EtOAc (3 × 50 mL), and the combined organic layer was washed with brine and dried with anhydrous Na_2SO_4. The solvent was removed under a vacuum, and the residue was purified by silica gel chromatography to give products **2** or **3**.

Gram-Scale Study for Preparation of Compound 2a. *N*-Arylpropynamide **1a** (1g, 4.25 mmol, 1.0 equiv) was added to a mixture of toluene (4 mL) and DMSO (4 mL) in a flask with a stir bar, and then $SOCl_2$ (8.5 mmol, 2.0 equiv) was added dropwise at room temperature. Then the mixture was stirred at 50 °C (oil bath) until the substrate was completely consumed. The mixture was cooled to room temperature and was treated with saturated aq. $NaHCO_3$ (40 mL). The mixture was extracted with EtOAc (60 mL × 3), and the combined organic layer was washed with brine and dried with anhydrous Na_2SO_4. After purification by silica gel chromatography (10% EtOAc/PE), product **2a** was obtained in 80% yield (956.7 mg), a white solid.

1-Methyl-3-(methylthio)-4-phenylquinolin-2(1H)-one (2a). Following the general procedure, product **2a** was synthesized. After purification by silica gel chromatography (10% EtOAc/PE), product **2a** was obtained in 86% yield (120.9 mg), a white solid, mp 130−132 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55−7.47 (m, 4H), 7.40 (d, J = 8.4 Hz, 1H), 7.26−7.24 (m, 2H), 7.13 (dd, J = 8.1, 1.7 Hz, 1H), 7.11−7.08 (m, 1H), 3.84 (s, 3H), 2.36 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.6, 152.0, 139.2, 137.2, 130.3, 128.9, 128.6, 128.4, 128.2, 122.1, 121.4, 114.1, 30.5, 17.5. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{17}H_{16}NOS^+$ 282.0947, found 282.0948.

1,5,7-Trimethyl-3-(methylthio)-4-phenylquinolin-2(1H)-one (2b). Following the general procedure, product **2b** was synthesized. After purification by silica gel chromatography (10% EtOAc/PE), product **2b** was obtained in 87% yield (134.6 mg), a white solid, mp 132−134 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.47−7.40 (m, 3H), 7.22−7.16 (m, 2H), 7.12 (s, 1H), 6.78 (s, 1H), 3.83 (s, 3H), 2.42 (s, 3H), 2.33 (s, 3H), 1.70 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 179.6, 167.9, 153.7, 148.5, 146.2, 132.9, 132.2, 131.3, 129.5, 128.4, 128.3, 111.7, 68.9, 55.5, 25.9, 14.9. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{19}H_{20}NOS^+$ 310.1260, found 310.1264.

6-(tert-Butyl)-1-methyl-3-(methylthio)-4-phenylquinolin-2(1H)-one (2c). Following the general procedure, product **2c** was synthesized. After purification by silica gel chromatography (10% EtOAc/PE), product **2c** was obtained in 88% yield (148.5 mg), a white solid, mp 138−140 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (dd, J = 8.8, 2.3 Hz, 1H), 7.55−7.47 (m, 3H), 7.35 (d, J = 8.9 Hz, 1H), 7.27 (d, J = 1.8 Hz, 1H), 7.25 (t, J = 1.4 Hz, 1H), 7.11 (d, J = 2.2 Hz, 1H), 3.83 (s, 3H), 2.35 (s, 3H), 1.19 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.6, 152.4, 144.9, 137.3, 137.2, 128.9, 128.3, 128.2, 128.1, 124.6, 120.9, 113.9, 34.3, 31.2, 30.4, 17.6. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{21}H_{24}NOS^+$ 338.1573, found 338.1576.

7-Methoxy-1-methyl-3-(methylthio)-4-phenylquinolin-2(1H)-one (2d). Following the general procedure, product **2d** was synthesized. After purification by silica gel chromatography (10% EtOAc/PE), product **2d** was obtained in 66% yield (102.1 mg), a white solid, mp 110−112 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56−7.46 (m, 3H), 7.27−7.22 (m, 2H), 7.06 (d, J = 9.0 Hz, 1H), 6.84 (d, J = 2.3 Hz, 1H), 6.71 (dd, J = 9.0, 2.4 Hz, 1H), 3.93 (s, 3H), 3.82 (s, 3H), 2.35 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 161.55, 161.14, 152.73, 141.01, 137.51, 130.15, 128.77, 128.33, 128.13, 124.83, 115.68, 109.47, 98.51, 55.63, 30.54, 17.56. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{18}H_{18}NO_2S^+$ 312.1053, found 312.1056.

5-Methoxy-1-methyl-3-(methylthio)-4-phenylquinolin-2(1H)-one (2d'). Following the general procedure, product **2d'** was synthesized. After purification by silica gel chromatography (10% EtOAc/PE), product **2d'** was obtained in 22% yield (35.2 mg), a yellow solid, mp 154−156 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 (t, J = 8.4 Hz, 1H), 7.41−7.37 (m, 2H), 7.36−7.32 (m, 1H), 7.12 (dt, J = 3.0, 1.8 Hz, 2H), 7.02 (d, J = 8.6 Hz, 1H), 6.58 (d, J = 8.1 Hz, 1H), 3.82 (s, 3H), 3.29 (s, 3H), 2.33 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 163.4, 158.0, 153.6, 142.5, 133.8, 131.4, 128.9, 128.8, 128.7, 128.6, 128.1, 114.5, 110.4, 98.5, 55.8, 37.4, 29.6. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{18}H_{18}NO_2S^+$ 312.1053, found 312.1057.

5-Fluoro-1-methyl-3-(methylthio)-4-phenylquinolin-2(1H)-one (2e). Following the general procedure, product **2e** was synthesized. After purification by silica gel chromatography (10% EtOAc/PE), product **2e** was obtained in 63% yield (94.3 mg), a white solid, mp 138−140 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51−7.28 (m, 4H), 7.14 (dd, J = 7.3, 1.9 Hz, 3H), 6.71 (dd, J = 11.7, 8.1 Hz, 1H), 3.75 (s, 3H), 2.29 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.1, 159.2 (d, J^1 = 255.6 Hz), 148.1 (d, J = 2.3 Hz), 140.5 (d, J^4 = 4.4 Hz), 139.8 (d, J^4 = 4.1 Hz), 130.9 (d, J^3 = 10.7 Hz), 130.7, 127.9, 127.7, 127.3 (d, J^4 = 3.9 Hz), 110.7 (d, J^3 = 10.6 Hz), 110.3 (d, J^4 = 3.7 Hz), 109.5 (d, J^2 = 22.9 Hz), 31.3, 17.5. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{17}H_{15}{}^{19}FNOS^+$ 300.0853, found 300.0856.

6-Chloro-1-methyl-3-(methylthio)-4-phenylquinolin-2(1H)-one (2f). Following the general procedure, product **2f** was synthesized. After purification by silica gel chromatography (10% EtOAc/PE), product **2f** was obtained in 58% yield (91.6 mg), a white solid, mp 122−124 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56−7.49 (m, 3H), 7.46 (dd, J = 9.0, 2.4 Hz, 1H), 7.33 (d, J = 9.0 Hz, 1H), 7.25−7.20 (m, 2H), 7.07 (d, J = 2.4 Hz, 1H), 3.81 (s, 3H), 2.35 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 160.2, 150.3, 137.7, 136.5, 130.4, 130.1, 128.8, 128.7, 128.5, 127.7, 127.3, 122.5, 115.5, 30.6, 17.3. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{17}H_{15}{}^{35}ClNOS^+$ 316.0557, found 316.0559.

4-(4-Bromophenyl)-1-methyl-3-(methylthio)quinolin-2(1H)-one (2g). Following the general procedure, product **2g** was synthesized. After purification by silica gel chromatography (10% EtOAc/PE), product **2g** was obtained in 60% yield (117.1 mg), a pale-yellow solid, mp 112−114 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57−7.50 (m, 3H), 7.47 (dd, J = 9.0, 2.4 Hz, 1H), 7.33 (d, J = 9.0 Hz, 1H), 7.23 (dd, J = 7.6, 1.7 Hz, 2H), 7.08 (d, J = 2.4 Hz, 1H), 3.82 (s, 3H), 2.36 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.2, 150.4, 137.6, 136.5, 132.9, 130.4, 130.2, 128.8, 128.7, 128.6, 127.7, 127.3, 122.5, 115.8, 115.5, 30.7, 17.4. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{17}H_{15}{}^{79}BrNOS^+$ 360.0052, found 360.0054.

1-Methyl-3-(methylthio)-4-phenyl-6-(trifluoromethyl)quinolin-2(1H)-one (2h). Following the general procedure, product **2h** was synthesized. After purification by silica gel chromatography (10% EtOAc/PE), product **2h** was obtained in 76% yield (132.8 mg), a white solid, mp 104−106 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.73 (d, J = 8.8 Hz, 1H), 7.58−7.51 (m, 3H), 7.49 (d, J = 8.8 Hz, 1H), 7.38 (s, 1H), 7.26−7.22 (m, 2H), 3.86 (s, 3H), 2.36 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 160.4, 150.8, 141.0, 136.1, 130.7, 128.8, 128.7, 128.6, 126.4 (q, J^3 = 3.1 Hz), 125.4 (q, J^3 = 3.9 Hz), 124.3 (q, J^2 = 32.9 Hz), 123.9 (q, J^1 = 269.9 Hz), 121.1, 114.6, 30.7, 17.3. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{18}H_{15}{}^{19}F_3NOS^+$ 350.0821, found 350.0825.

1-Methyl-3-(methylthio)-4-phenylbenzo[h]quinolin-2(1H)-one (2i). Following the general procedure, product **2i** was synthesized. After purification by silica gel chromatography (10% EtOAc/PE), product **2i** was obtained in 69% yield (116.0 mg), a white solid, mp 128−130 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.44 (d, J = 8.2 Hz, 1H), 7.88−7.82 (m, 1H), 7.60−7.48 (m, 5H), 7.45 (d, J = 8.8 Hz, 1H), 7.27 (d, J = 1.3 Hz, 2H), 7.10 (d, J = 8.7 Hz, 1H), 4.15 (s, 3H), 2.41 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 162.8, 151.8, 138.6, 137.4, 135.1, 129.0, 128.6, 128.5, 128.3, 128.1, 127.4, 125.8, 125.1, 124.2, 123.6, 123.4, 119.1, 41.3, 17.3. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{21}H_{18}NOS^+$ 332.1104, found 332.1106.

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*1-Methyl-3-(methylthio)-4-(p-tolyl)quinolin-2(1H)-one (**2j**).* Following the general procedure, product **2j** was synthesized. After purification by silica gel chromatography (10% EtOAc/PE), product **2j** was obtained in 80% yield (118.2 mg), a white solid, mp 104−106 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54−7.50 (m, 1H), 7.39 (d, J = 8.5 Hz, 1H), 7.33 (d, J = 7.8 Hz, 2H), 7.16 (dd, J = 8.1, 1.3 Hz, 1H), 7.14 (d, J = 7.9 Hz, 2H), 7.09 (t, J = 7.6 Hz, 1H), 3.83 (s, 3H), 2.47 (s, 3H), 2.36 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 160.7, 152.1, 139.2, 138.0, 134.3, 130.2, 129.1, 128.8, 128.7, 128.5, 121.9, 121.6, 114.0, 30.4, 21.5, 17.5. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{18}H_{18}NOS^+$ 296.1104, found 296.1107.

*4-(4-Methoxyphenyl)-1-methyl-3-(methylthio)quinolin-2(1H)-one (**2k**).* Following the general procedure, product **2k** was synthesized. After purification by silica gel chromatography (10% EtOAc/PE), product **2k** was obtained in 81% yield (126.1 mg), a white solid, mp 108−110 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54−7.48 (m, 1H), 7.39 (d, J = 8.5 Hz, 1H), 7.21−7.15 (m, 3H), 7.10 (dd, J = 7.9, 7.2 Hz, 1H), 7.05 (d, J = 8.3 Hz, 2H), 3.89 (s, 3H), 3.83 (s, 3H), 2.36 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 160.6, 159.5, 151.6, 139.2, 130.3, 130.2, 129.4, 128.9, 128.5, 121.9, 121.7, 114.0, 113.8, 55.3, 30.4, 17.5. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{18}H_{18}NO_2S^+$ 312.1053, found 312.1056.

*4-(4-Chlorophenyl)-1-methyl-3-(methylthio)quinolin-2(1H)-one (**2l**).* Following the general procedure, product **2l** was synthesized. After purification by silica gel chromatography (10% EtOAc/PE), product **2l** was obtained in 81% yield (127.9 mg), a white solid, mp 140−142 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 (ddd, J = 8.4, 6.6, 1.8 Hz, 1H), 7.50 (d, J = 8.1 Hz, 2H), 7.41 (d, J = 8.5 Hz, 1H), 7.19 (d, J = 8.2 Hz, 2H), 7.14−7.07 (m, 2H), 3.83 (s, 3H), 2.38 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 160.4, 150.8, 139.3, 135.6, 134.3, 130.5, 130.3, 128.9, 128.8, 128.1, 122.2, 121.1, 114.2, 30.5, 17.4. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{17}H_{15}{}^{35}ClNOS^+$ 316.0557, found 316.0558.

*4-(4-Bromophenyl)-1-methyl-3-(methylthio)quinolin-2(1H)-one (**2m**).* Following the general procedure, product **2m** was synthesized. After purification by silica gel chromatography (10% EtOAc/PE), product **2m** was obtained in 79% yield (142.3 mg), a white solid, mp 170−172 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.69−7.65 (m, 2H), 7.63 (dd, J = 8.1, 1.8 Hz, 1H), 7.46 (d, J = 8.6 Hz, 1H), 7.27 (d, J = 2.0 Hz, 1H), 7.21−7.16 (m, 2H), 7.05 (dd, J = 8.1, 2.1 Hz, 1H), 3.81 (s, 3H), 3.13 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 157.8, 151.9, 140.4, 132.7, 132.1, 131.7, 131.4, 130.5, 130.5, 129.0, 123.4, 122.8, 120.6, 114.5, 38.6, 29.6. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{17}H_{15}{}^{79}BrNOS^+$ 360.0052, found 360.0056.

*4-(2-Bromophenyl)-1-methyl-3-(methylthio)quinolin-2(1H)-one (**2n**).* Following the general procedure, product **2n** was synthesized. After purification by silica gel chromatography (10% EtOAc/PE), product **2n** was obtained in 78% yield (140.5 mg), a white solid, mp 124−126 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75 (t, J = 6.3 Hz, 1H), 7.55 (t, J = 7.2 Hz, 1H), 7.46 (t, J = 7.5 Hz, 1H), 7.42 (d, J = 8.5 Hz, 1H), 7.38−7.33 (m, 1H), 7.21−7.16 (m, 1H), 7.12 (t, J = 7.5 Hz, 1H), 6.96 (d, J = 8.0 Hz, 1H), 3.85 (s, 3H), 2.45 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 160.5, 150.8, 139.3, 138.3, 132.9, 130.5, 129.8, 129.1, 127.6, 127.6, 122.8, 122.3, 120.4, 114.3, 30.5, 16.9. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{17}H_{15}{}^{79}BrNOS^+$ 360.0052, found 360.0053.

*Methyl 2-(1-methyl-3-(methylthio)-2-oxo-1,2-dihydroquinolin-4-yl)benzoate (**2o**).* Following the general procedure, product **2o** was synthesized. After purification by silica gel chromatography (10% EtOAc/PE), product **2o** was obtained in 82% yield (139.2 mg), a white solid, mp 142−144 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (dd, J = 7.9, 1.1 Hz, 1H), 7.67 (td, J = 7.5, 1.4 Hz, 1H), 7.57 (td, J = 7.7, 1.3 Hz, 1H), 7.51 (ddd, J = 8.5, 7.1, 1.5 Hz, 1H), 7.40 (d, J = 8.2 Hz, 1H), 7.18 (dd, J = 7.6, 0.9 Hz, 1H), 7.10−7.02 (m, 1H), 6.92 (dd, J = 8.1, 1.3 Hz, 1H), 3.84 (s, 3H), 3.64 (s, 3H), 2.33 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 166.2, 160.6, 153.2, 139.2, 138.9, 132.5, 130.6, 130.2, 129.4, 128.4, 127.6, 126.9, 122.1, 121.3, 114.2, 52.0, 30.4, 16.9. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{19}H_{18}NO_3S^+$ 340.1002, found 340.1004.

*1-Methyl-3-(methylthio)quinolin-2(1H)-one (**2p**).* Following the general procedure, product **2p** was synthesized. After purification by silica gel chromatography (10% EtOAc/PE), product **2p** was obtained in 62% yield (63.6 mg), a white oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.32 (m, 4H), 5.85 (s, 1H), 3.37 (s, 3H), 2.25 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 164.82, 142.27, 134.49, 128.99, 128.07, 126.54, 116.26, 37.01, 17.04. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{11}H_{12}NOS^+$ 206.0634, found 206.0636.

*4-([1,1′-Biphenyl]-4-yl)-1-ethyl-3-(methylthio)quinolin-2(1H)-one (**2q**).* Following the general procedure, product **2q** was synthesized. After purification by silica gel chromatography (10% EtOAc/PE), product **2q** was obtained in 84% yield (156.0 mg), a pale-yellow solid, mp 220−222 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78−7.74 (m, 2H), 7.70 (dt, J = 8.2, 1.7 Hz, 2H), 7.54 (ddd, J = 8.6, 7.1, 1.5 Hz, 1H), 7.51−7.46 (m, 2H), 7.44 (d, J = 8.3 Hz, 1H), 7.41−7.36 (m, 1H), 7.35−7.31 (m, 2H), 7.22 (dd, J = 8.1, 1.4 Hz, 1H), 7.14−7.07 (m, 1H), 4.48 (q, J = 7.1 Hz, 2H), 2.40 (s, 3H), 1.46 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.0, 151.5, 140.9, 140.5, 138.2, 136.2, 130.3, 129.4, 128.9, 128.7, 127.6, 127.2, 127.1, 121.9, 121.7, 113.9, 38.4, 17.4, 12.7. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{24}H_{22}NOS^+$ 372.1417, found 372.1418.

*1-Isopropyl-3-(methylthio)-4-phenylquinolin-2(1H)-one (**2r**).* Following the general procedure, product **2r** was synthesized. After purification by silica gel chromatography (10% EtOAc/PE), product **2r** was obtained in 80% yield (123.8 mg), a pale-yellow solid, mp 160−162 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 8.7 Hz, 1H), 7.54−7.44 (m, 4H), 7.26−7.23 (m, 2H), 7.12 (dd, J = 8.1, 1.6 Hz, 1H), 7.07−7.02 (m, 1H), 2.32 (s, 3H), 1.73 (s, 3H), 1.72 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.8, 151.5, 137.4, 129.5, 128.9, 128.8, 128.4, 128.1, 122.2, 121.5, 114.6, 19.8, 17.4. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{19}H_{20}NOS^+$ 310.1260, found 310.1265.

*3-(Methylthio)-1,4-diphenylquinolin-2(1H)-one (**2s**).* Following the general procedure, product **2s** was synthesized. After purification by silica gel chromatography (10% EtOAc/PE), product **2s** was obtained in 82% yield (140.8 mg), a white solid, mp 216−218 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (dd, J = 10.4, 4.7 Hz, 2H), 7.59−7.51 (m, 4H), 7.36 (dd, J = 5.2, 3.2 Hz, 2H), 7.34−7.31 (m, 2H), 7.31−7.26 (m, 1H), 7.14 (dd, J = 8.1, 1.4 Hz, 1H), 7.08−7.02 (m, 1H), 6.69 (d, J = 8.5 Hz, 1H), 2.41 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.5, 152.0, 140.2, 138.0, 137.2, 130.3, 129.7, 129.1, 129.0, 128.9, 128.8, 128.6, 128.3, 127.9, 122.3, 121.2, 115.9, 100.0, 17.3. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{22}H_{18}NOS^+$ 344.1104, found 344.1106.

*6-(Methylthio)-7-phenyl-2,3-dihydro-1H,5H-pyrido[3,2,1-ij]-quinolin-5-one (**2t**).* Following the general procedure, product **2t** was synthesized. After purification by silica gel chromatography (10% EtOAc/PE), product **2t** was obtained in 80% yield (123.0 mg), a white solid, mp 120−122 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.53−7.49 (m, 2H), 7.49−7.45 (m, 1H), 7.27 (d, J = 1.3 Hz, 1H), 7.25−7.22 (m, 2H), 7.00−6.93 (m, 2H), 4.40−4.19 (m, 2H), 3.02 (t, J = 6.2 Hz, 2H), 2.36 (s, 3H), 2.17 (dt, J = 12.1, 6.1 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 160.1, 151.8, 137.6, 135.9, 129.6, 128.8, 128.4, 128.2, 128.1, 126.4, 124.6, 121.5, 121.3, 43.3, 27.8, 20.8, 17.4. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{19}H_{18}NOS^+$ 308.1104, found 308.1106.

*6-(tert-Butyl)-1-methyl-3-((methyl-d_3)thio)-4-phenylquinolin-2(1H)-one (**2u**).* Following the general procedure, product **2u** was synthesized. After purification by silica gel chromatography (10% EtOAc/PE), product **2u** was obtained in 81% yield (139.6 mg), a white solid, mp 138−140 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (dd, J = 8.8, 2.3 Hz, 1H), 7.55−7.46 (m, 3H), 7.35 (d, J = 8.9 Hz, 1H), 7.27 (d, J = 1.7 Hz, 1H), 7.26−7.23 (m, 1H), 7.11 (d, J = 2.2 Hz, 1H), 3.83 (s, 3H), 1.19 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.6, 152.3, 144.9, 137.3, 137.2, 128.9, 128.4, 128.3, 128.2, 128.1, 124.6, 121.0, 1139, 34.3, 31.2, 30.4. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{21}H_{21}D_3NOS^+$ 341.1761, found 341.1764.

*1-Methyl-3-(methylthio)-4-phenyl-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione (**3a**).* Following the general procedure, product **3a** was synthesized. After purification by silica gel chromatography (15%

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EtOAc/PE), product **3a** was obtained in 87% yield (129.4 mg), a white solid, mp 162−164 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38−7.32 (m, 3H), 7.32−7.28 (m, 2H), 6.53−6.48 (m, 2H), 6.47−6.41 (m, 2H), 2.90 (s, 3H), 2.40 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 183.9, 168.3, 147.4, 145.5, 133.7, 133.0, 131.2, 129.5, 128.4, 128.3, 67.5, 26.1, 14.8. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{17}H_{16}NO_2S^+$ 298.0896, found 298.0898.

When *N*-(4-methoxyphenyl)-*N*-methyl-3-phenylpropiolamide was used as the substrate, product **3a** was obtained in 85% yield (126.3 mg). When *N*-methyl-3-phenyl-*N*-(4-(trifluoromethoxy)phenyl)-propiolamide was used as the substrate, product **3a** was obtained in 82% yield (122.0 mg).

*1-Methyl-3-(methylthio)-4-(p-tolyl)-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione (**3b**).* Following the general procedure, product **3b** was synthesized. After purification by silica gel chromatography (15% EtOAc/PE), product **3b** was obtained in 85% yield (132.1 mg), a white solid, mp 130−132 °C ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.20 (d, J = 8.1 Hz, 2H), 7.14 (d, J = 7.7 Hz, 2H), 6.49 (d, J = 10.1 Hz, 2H), 6.44 (dd, J = 10.2, 1.3 Hz, 2H), 2.89 (s, 3H), 2.42 (s, 3H), 2.34 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 184.1, 168.4, 147.8, 145.6, 139.8, 132.9, 129.1, 128.2, 67.4, 26.1, 21.3, 14.9. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{18}H_{18}NO_2S^+$ 312.1053, found 312.1056.

When *N*-(4-methoxyphenyl)-*N*-methyl-3-(*p*-tolyl)propiolamide was used as the substrate, product **3b** was obtained in 86% yield (133.9 mg).

*4-(4-Methoxyphenyl)-1-methyl-3-(methylthio)-1-azaspiro[4.5]-deca-3,6,9-triene-2,8-dione (**3c**).* Following the general procedure, product **3c** was synthesized. After purification by silica gel chromatography (15% EtOAc/PE), product **3c** was obtained in 85% yield (139.1 mg), a white solid, mp 120−122 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.20 (d, J = 8.1 Hz, 2H), 7.14 (d, J = 7.9 Hz, 2H), 6.49 (d, J = 10.2 Hz, 2H), 6.44 (d, J = 10.2 Hz, 2H), 2.89 (s, 3H), 2.42 (s, 3H), 2.34 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 184.1, 168.4, 147.8, 145.6, 139.8, 133.1, 132.9, 129.1, 128.2, 128.2, 67.4, 26.1, 21.3, 14.9. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{18}H_{18}NO_3S^+$ 328.1002, found 328.1004.

When *N*,3-bis(4-methoxyphenyl)-*N*-methylpropiolamide was used as the substrate, product **3c** was obtained in 83% yield (135.9 mg).

*Methyl 4-(1-methyl-3-(methylthio)-2,8-dioxo-1-azaspiro[4.5]-deca-3,6,9-trien-4 -yl)benzoate (**3d**).* Following the general procedure, product **3d** was synthesized. After purification by silica gel chromatography (15% EtOAc/PE), product **3d** was obtained in 81% yield (144.3 mg), a white solid, mp 162−164 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 (dd, J = 8.5, 1.8 Hz, 2H), 7.38 (dd, J = 8.4, 1.2 Hz, 2H), 6.49 (d, J = 10.2 Hz, 2H), 6.45 (dd, J = 10.2, 1.8 Hz, 2H), 3.91 (s, 3H), 2.90 (s, 3H), 2.43 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 183.7, 167.8, 166.2, 145.7, 145.1, 135.7, 135.1, 133.2, 131.0, 129.6, 128.5, 67.3, 52.3, 26.2, 14.7. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{19}H_{18}NO_4S^+$ 356.0951, found 356.0952.

When methyl 4-(3-((4-methoxyphenyl)(methyl)amino)-3-oxoprop-1-yn-1-yl)-benzoate was used as the substrate, product **3d** was obtained in 82% yield (145.7 mg).

*1-Methyl-3-(methylthio)-4-(4-nitrophenyl)-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione (**3e**).* Following the general procedure, product **3e** was synthesized. After purification by silica gel chromatography (15% EtOAc/PE), product **3e** was obtained in 83% yield (143.1 mg), a pale-yellow solid, mp 160−162 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.21 (dq, J = 9.1, 2.0 Hz, 2H), 7.59−7.42 (m, 2H), 6.61−6.35 (m, 4H), 2.91 (s, 3H), 2.52 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 183.4, 167.4, 148.1, 144.7, 144.0, 137.7, 136.4, 133.5, 129.4, 123.7, 67.1, 26.2, 14.6. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{17}H_{15}N_2O_4S^+$ 343.0747, found 343.0748.

When *N*-(4-methoxyphenyl)-*N*-methyl-3-(4-nitrophenyl)-propiolamide was used as the substrate, product **3e** was obtained in 80% yield (136.9 mg).

*1-Methyl-3-(methylthio)-4-(thiophen-2-yl)-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione (**3f**).* Following the general procedure, product **3f** was synthesized. After purification by silica gel chromatography (15% EtOAc/PE), product **3f** was obtained in 79% yield (119.8 mg), a white solid, mp 138−140 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (dd, J = 5.1, 1.1 Hz, 1H), 7.42 (dd, J = 3.8, 1.1 Hz, 1H), 7.05 (dd, J = 5.1, 3.9 Hz, 1H), 6.61−6.56 (m, 2H), 6.55−6.49 (m, 2H), 2.86 (s, 3H), 2.72 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 184.2, 168.1, 146.2, 141.8, 133.2, 133.1, 129.4, 129.2, 129.1, 127.2, 65.7, 25.6, 15.3. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{15}H_{14}NO_2S_2^+$ 304.0460, found 304.0462.

When *N*-(4-methoxyphenyl)-*N*-methyl-3-(thiophen-2-yl)-propiolamide was used as the substrate, product **3f** was obtained in 81% yield (122.9 mg).

*7-Chloro-1-methyl-3-(methylthio)-4-phenyl-1-azaspiro[4.5]-deca-3,6,9-triene-2,8-dione (**3g**).* Following the general procedure, product **3g** was synthesized. After purification by silica gel chromatography (15% EtOAc/PE), product **3g** was obtained in 82% yield (127.8 mg), a white solid, mp 176−178 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, J = 5.1 Hz, 3H), 7.27−7.21 (m, 2H), 6.73 (s, 1H), 6.52 (q, J = 9.9 Hz, 2H), 2.93 (s, 3H), 2.38 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 177.2, 167.9, 146.1, 145.9, 141.3, 136.1, 134.2, 131.8, 130.7, 129.8, 128.6, 128.4, 69.3, 26.5, 14.7. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{17}H_{15}{}^{35}ClNO_2S^+$ 332.0507, found 332.0508.

*7-Methoxy-1-methyl-3-(methylthio)-4-phenyl-1-azaspiro[4.5]-deca-3,6,9-triene-2,8-dione (**3h**).* Following the general procedure, product **3h** was synthesized. After purification by silica gel chromatography (15% EtOAc/PE), product **3h** was obtained in 81% yield (133.4 mg), a white solid, mp 156−158 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.31 (m, 3H), 7.29−7.25 (m, 3H), 6.49 (dd, J = 9.8, 2.5 Hz, 1H), 6.44 (d, J = 9.8 Hz, 1H), 5.35 (d, J = 2.5 Hz, 1H), 3.66 (s, 3H), 2.89 (s, 3H), 2.40 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 179.6, 167.9, 153.7, 148.5, 146.2, 132.9, 132.2, 131.3, 129.5, 128.4, 128.3, 111.7, 68.9, 55.5, 25.9, 14.9. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{18}H_{18}NO_3S^+$ 328.1002, found 328.1004.

*6-Iodo-1-methyl-3-(methylthio)-4-phenyl-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione (**3i**).* Following the general procedure, product **3i** was synthesized. After purification by silica gel chromatography (15% EtOAc/PE), product **3i** was obtained in 81% yield (173.5 mg), a light yellow solid, mp 114−116 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (dd, J = 5.8, 1.7 Hz, 3H), 7.32 (d, J = 6.7 Hz, 2H), 7.20 (s, 1H), 6.80 (d, J = 9.8 Hz, 1H), 6.54 (d, J = 9.8 Hz, 1H), 2.84 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.0, 168.1, 146.8, 144.7, 144.5, 135.6 132.0, 130.4, 129.8, 128.5, 128.5, 126.2, 71.8, 25.9, 14.9. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{17}H_{15}INO_2S^+$423.9863, found 423.9867.

*1,6-Dimethyl-3-(methylthio)-4-phenyl-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione (**3j**).* Following the general procedure, product **3j** was synthesized. After purification by silica gel chromatography (15% EtOAc/PE), product **3j** was obtained in 78% yield (121.4 mg), a white solid, mp 118−120 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 (t, J = 5.1 Hz, 3H), 7.30 (d, J = 2.5 Hz, 2H), 6.53−6.40 (m, 2H), 6.32 (d, J = 4.4 Hz, 1H), 2.80 (s, 3H), 2.45 (s, 3H), 1.73 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 184.7, 168.7, 153.7, 147.9, 145.7, 133.9, 132.5, 131.9, 131.0, 129.7, 128.5, 128.0, 69.5, 25.7, 17.7, 15.1. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{18}H_{18}NO_2S^+$312.1053, found 312.1056.

*1-Methyl-3-(methylthio)-4-phenyl-1-azaspiro[4.5]deca-3,7,9-triene-2,6-dione (**3k**).* Following the general procedure, product **3k** was synthesized. After purification by silica gel chromatography (15% EtOAc/PE), product **3k** was obtained in 79% yield (118.2 mg), a white solid, mp 120−122 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39−7.30 (m, 3H), 7.23 (dd, J = 8.0, 1.4 Hz, 2H), 6.99 (ddd, J = 9.9, 6.0, 1.6 Hz, 1H), 6.50 (dd, J = 9.4, 5.9 Hz, 1H), 6.18 (d, J = 9.9 Hz, 1H), 6.12 (d, J = 9.1 Hz, 1H), 2.79 (s, 3H), 2.42 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 195.5, 169.7, 148.3, 141.8, 138.4, 133.1, 131.3, 129.3, 128.3, 128.2, 128.1, 127.5, 126.7, 74.9, 26.6, 14.9. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{17}H_{16}NO_2S^+$ 298.0896, found 298.0898.

*1-Methyl-3-((methyl-d_3)thio)-4-(p-tolyl)-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione (**3l**).* Following the general procedure, product **3l** was synthesized. After purification by silica gel chromatography (15% EtOAc/PE), product **3l** was obtained in 76% yield (119.0 mg), a white solid, mp 130−132 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (d, J = 8.2 Hz, 2H), 7.14 (d, J = 8.2 Hz, 2H), 6.47 (q, J = 10.3 Hz,

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4H), 2.89 (s, 3H), 2.34 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 184.2, 168.4, 147.8, 145.7, 139.8, 132.9, 129.1, 128.2, 67.4, 26.1, 21.4. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{18}H_{15}D_3NO_2S^+$ 315.1241, found 315.1243.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00775.

Spectral data for all new compounds, X-ray structures and data of **2a**, and computational data (PDF)

Accession Codes

CCDC 2024958 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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