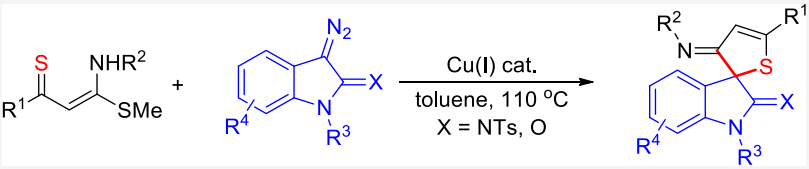
JOC The Journal of Organic Chemistry

pubs.acs.org/joc Article

Copper-Catalyzed [4 + 1] Annulation of Enaminothiones with Indoline-Based Diazo Compounds

Zilong Huang, Yuan He, Liandi Wang, Jiying Li, Bao-Hua Xu, Yong-Gui Zhou,* and Zhengkun Yu*

Cite This: J. Org. Chem. 2022, 87, 4424−4437 Read Online



ABSTRACT: A concise synthetic route to spiroindoline-fused *S*-heterocycles was developed through copper-catalyzed [4 + 1] annulation using enaminothiones as donor−acceptor synthons. Both 3-diazoindolin-2-imines and 3-diazooxindoles were amenable to work as effective C1 building blocks. The reaction proceeds *via* a copper-catalyzed cascade process involving the *in situ* generation of copper(I) carbene and C−S/C−C bond formation. This synthetic protocol features the use of readily available substrates, diverse substituent tolerance, and good to excellent yields.

■ INTRODUCTION

Transition-metal-catalyzed cross-coupling *via* transient metal carbenes has been used as a powerful tool in modern organic synthesis.[1] Metal carbenes generated *in situ* from transition-metal compounds and diazo to furnish a catalytic cycle have been employed in many transformations such as cyclopropanation, X−H (X = C, Si, O, S, N, etc.) insertions, ylide formation, 1,2-migration, and others.[2−4] In this regard, diazo compounds have advantages in building various carbo- and heterocyclic frameworks *via* metal carbene migratory insertion/intramolecular annulation sequences.[4,5] Spirocyclic indole derivatives have always attracted considerable attention from the synthetic community because the incorporation of spirocyclic scaffolds into pharmaceutical candidates usually impart increased pharmacokinetic properties.[6] It has been well known that sulfur-containing molecules are potential candidates for antibacterial, antiviral, and anticancer drugs.[7,8] In this context, the construction of spiroindoline-fused *S*-heterocycles, which are highly promising structural motifs pursued by both medicinal and synthetic chemists, has called for the development of new synthetic methodologies.[9−12] Recently, the readily available 3-diazooxindoles have been extensively applied for the construction of spirocyclic oxindole substructures that bear a quaternary carbon center at the C3 position.[6,13,14] In 2014, Wang and co-workers reported a new class of diazo compounds, that is, 3-diazoindolin-2-imines (indole-embedded α-diazo amidines), which were successfully applied as the precursors of transition-metal carbenes in various transition-metal-catalyzed cross-coupling reactions.[15]

Although transition-metal-catalyzed cycloaddition reactions have recently been well documented to access spirocyclic indoline derivatives from cyclic diazo compounds,[16−18] indole-embedded diazo compounds have seldom been used to prepare spiroindoline-fused *S*-heterocycles. Hu et al. reported the Rh(II)/chiral phosphoric acid-cocatalyzed enantioselective synthesis of spirooxindole-fused thiaindans from 2-mercaptophenyl ketones and 3-diazooxindoles (Scheme 1a).[9] Because such molecules are very important in drug discovery, efficient catalytic approaches for the rapid construction of spiro *S*-heterocyclic cores are in great demand. Alkylthio-substituted enaminones[19,20] and enaminothiones[21] have proven to be useful coupling partners to serve as donor−acceptor synthons in the construction of *O*- and *S*-heterocycles due to their unique structural characteristics.[20,21] We recently found that α-thioxo ketene *N*,*S*-acetals could react with ketone *N*-tosylhydrazones under copper catalysis, forming five-membered 2-imino *O*- and *S*-heterocycles *via* carbene insertion into the olefinic C═C bond (Scheme 1b).[21] Thus, we envisioned that such alkylthio-functionalized enaminothiones might also undergo the same type of carbene insertion/annulation cascade with indole-embedded diazo compounds. Unexpectedly, when ketone *N*-tosylhydrazones were replaced with 3-diazoindolin-2-imines, no carbene insertion into the olefinic C═C bond occurred, but a [4 + 1] annulation process was observed. Herein, we disclose a concise strategy for the rapid construction of spiroindoline-fused *S*-heterocycles by means of

Received: January 20, 2022
Published: March 9, 2022

https://doi.org/10.1021/acs.joc.2c00137
J. Org. Chem. 2022, 87, 4424−4437

Scheme 1. Diazo-Involved Approaches to *S*-Heterocycles

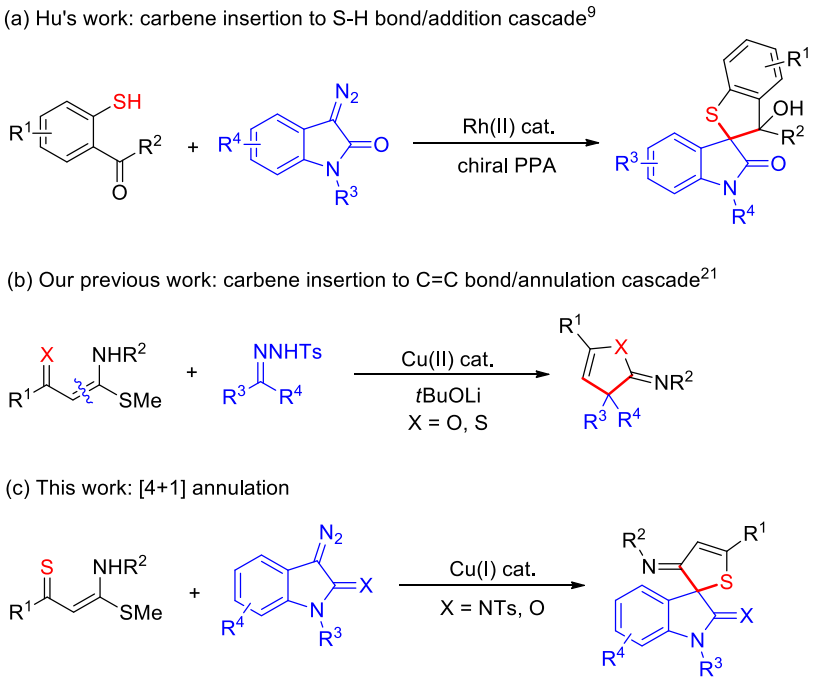
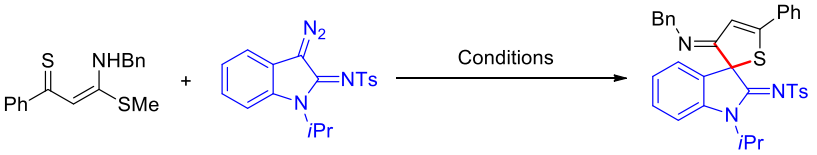


Table 1. Optimization of Reaction Conditions[a]



1a **2a** **3a**

entry	catalyst	solvent	temp. (°C)	yield[b] (%)
1	$CuBr_2$	toluene	110	32
2	CuOAc	toluene	110	26
3	CuI	toluene	110	47
4	CuCN	toluene	110	39
5	CuBr	toluene	110	56
6	$Cu(MeCN)_4BF_4$	toluene	110	82
7	$Cu(MeCN)_4BF_4$	toluene	100	67
8	$Cu(MeCN)_4BF_4$	toluene	120	73
9	$Cu(MeCN)_4BF_4$	dioxane	110	62
10	$Cu(MeCN)_4BF_4$	DCE	110	71
11[c]	$Cu(MeCN)_4BF_4$	toluene	110	70
12[d]	$Cu(MeCN)_4BF_4$	toluene	110	73
13[e]	$Cu(MeCN)_4BF_4$	toluene	110	65
14[f]	$Cu(MeCN)_4BF_4$	toluene	110	79
15[g]	$Cu(MeCN)_4BF_4$	toluene	110	84 (84)[h]

[a]Conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), catalyst (10 mol %), solvent (2.0 mL), 2 h, and 0.1 MPa N_2. [b]Determined by ^1H NMR analysis using 1,3,5-trimethoxybenzene as the internal standard. [c]**2a** (0.24 mmol). [d]**2a** (0.4 mmol). [e]$Cu(MeCN)_4BF_4$ (5 mol %). [f]$Cu(MeCN)_4BF_4$ (15 mol %). [g]**1a** (0.3 mmol) and **2a** (0.45 mmol). [h]Isolated yield given in parentheses. DCE = 1,2-dichloroethane.

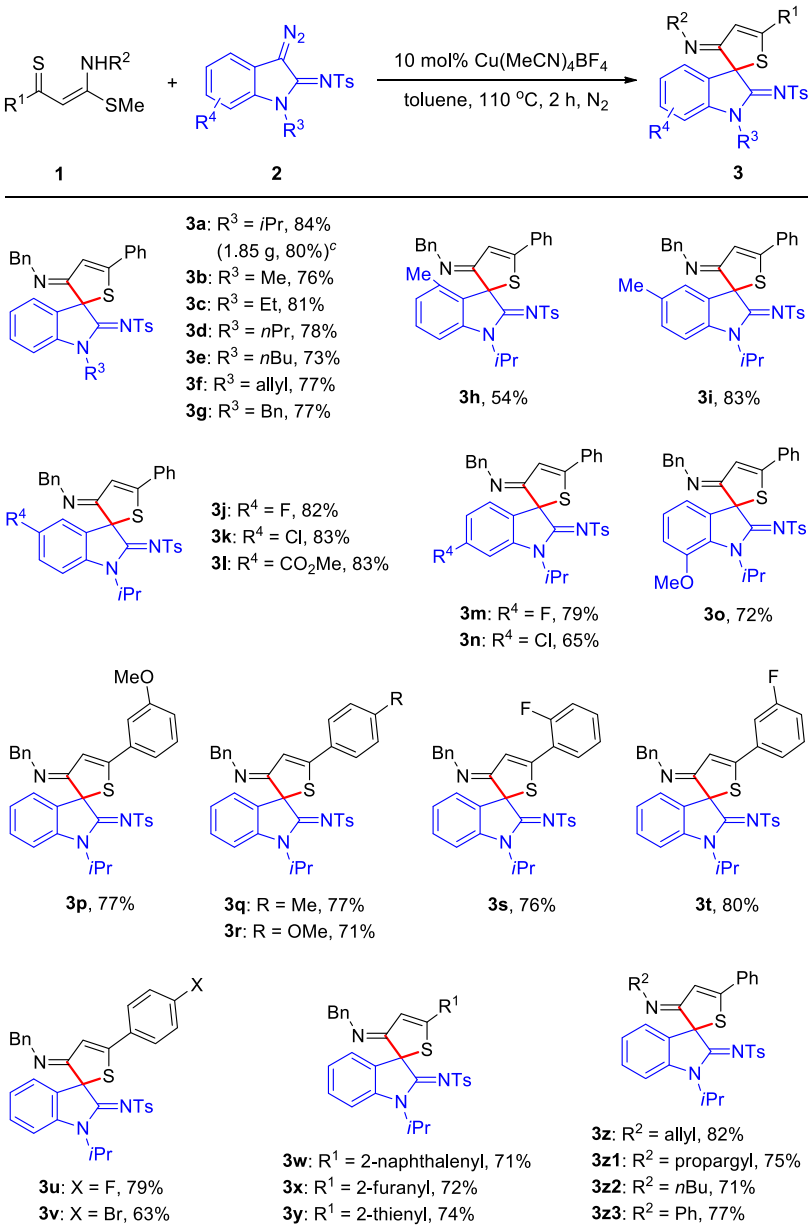
enaminothiones and indoline-based diazo compounds under copper(I) catalysis (Scheme 1c).

■ RESULTS AND DISCUSSION

Initially, the reaction of enaminothione, that is, α-thioxo ketene *N*,*S*-acetal (**1a**) and 3-diazoindolin-2-imine (**2a**), was performed to optimize the reaction conditions (Table 1). Under a nitrogen atmosphere, the treatment of **1a** and **2a** in a 1:1.5 molar ratio in the presence of 10 mol % $CuBr_2$ in refluxing toluene for 2 h formed the target product **3a** in 32% yield (Table 1, entry 1). Various copper(I) catalysts, i.e., CuOAc, CuI, CuCN, CuBr, and $Cu(MeCN)_4BF_4$, were then screened, leading to the target product in 26−82% yields (Table 1, entries 2−6), and only $Cu(MeCN)_4BF_4$ exhibited a high catalytic activity (82% yield) (Table 1, entry 6). One hundred and ten degree Celsius seems to be the appropriate reaction temperature (Table 1, entries 6−8), and toluene was tested as the most effective reaction medium among the screened

https://doi.org/10.1021/acs.joc.2c00137
J. Org. Chem. 2022, 87, 4424−4437

Table 2. Scopes of Enaminothiones and 3-Diazoindolin-2-imines[a,b,c]



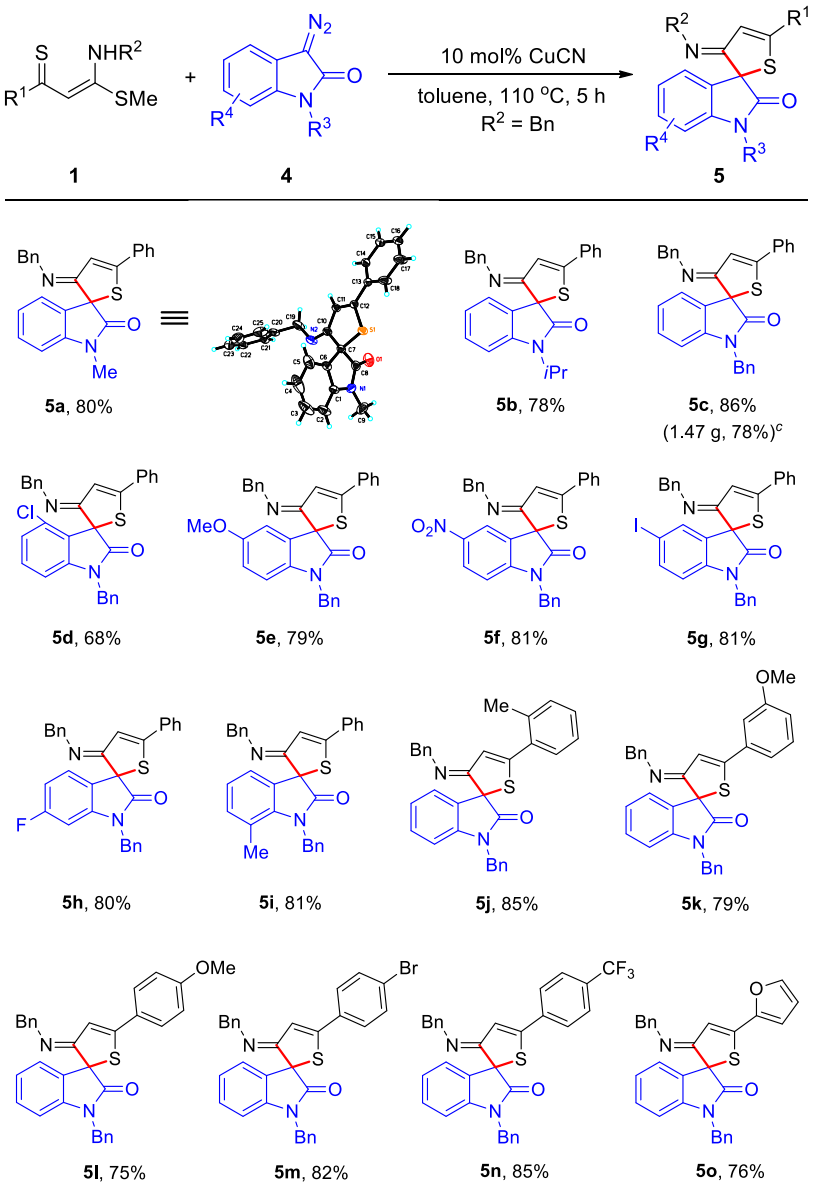
[a]Conditions: **1** (0.3 mmol), **2** (0.45 mmol), $Cu(MeCN)_4BF_4$ (0.03 mmol), toluene (2 mL), 110 °C, 2 h, and 0.1 MPa N_2. [b]Isolated yields. [c]**1a** (4.0 mmol) and **2a** (6.0 mmol).

solvents toluene, dioxane, and 1,2-dichloroethane (Table 1, entries 6, 9 and 10); 10 mol % was the best loading of $Cu(MeCN)_4BF_4$ (Table 1, entries 13−15). On a 0.3 mmol scale, the reaction gave **3a** in 84% isolated yield (Table 1, entries 11, 12, and 15). It is noteworthy that $Rh_2(OAc)_4$, $PdCl_2$, AgOAc, and $[Ir(COD)Cl]_2$ catalysts were ineffective for the desired reaction because the diazo compound could be readily decomposed under the stated conditions, and in the presence of 10 mol % chiral ligands such as (*R*)-Monophos, (*S*)-(−)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl, (*S*)-(−)-Segphos, or (*S*)-(+)-DTBM-Segphos, no asymmetric induction was observed (see the Supporting Information for details).

Next, the scopes of alkylthio-substituted enaminothiones (**1**) and 3-diazoindolin-2-imines (**2**) were explored (Table 2). The substituents on the nitrogen atom of the indole ring could be altered from isopropyl to methyl, ethyl, *n*-propyl, *n*-butyl, allyl, and benzyl, resulting in the corresponding products **3b**−**3g** (73−81%). An 80% isolated yield was achieved for the gram-scale synthesis of **3a** (1.85 g). The olefinic C═C double bond in enaminothione **1a** survived in all of the cases. It should be noted that *N*-unprotected and *N*-Boc (*tert*-butoxycarbonyl)-protected 3-diazoindolin-2-imines could not undergo the same type of reaction with **2a** under the stated conditions, which suggests that appropriate electron-donating capability of the *N*-heterocycle in 3-diazoindolin-2-imines is required to render the desired annulation process. An obvious steric effect was observed from 4-methyl, leading to the generation of **3h** in a relatively low yield (54%). However, no steric effect resulted from the substituents such as electron-donating methyl and electron-withdrawing fluoro, chloro, and ester groups at the 5-position, and thus, **3i**−**3l** were produced in 82−83% yields. 6-

https://doi.org/10.1021/acs.joc.2c00137
J. Org. Chem. 2022, 87, 4424−4437

Table 3. Scopes of Enaminothiones and 3-Diazooxindoles[a,b,c]



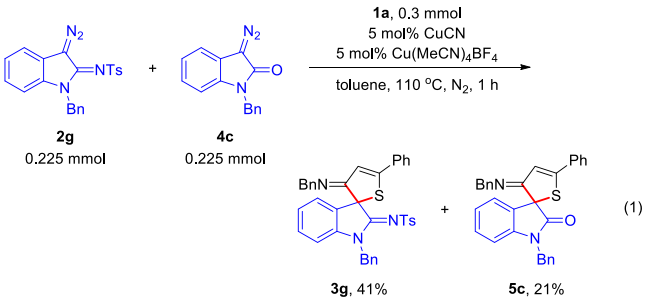
[a]Conditions: **1** (0.3 mmol), **4** (0.45 mmol), CuCN (0.03 mmol), toluene (3 mL), 110 °C, 5 h, and 0.1 MPa N_2. [b]Isolated yields. [c]**1a** (4.0 mmol), **2a** (6.0 mmol), 7 h. Perspective view of **5a** with thermal ellipsoids at the 50% probability level.

Fluoro had no obvious impact on the reaction efficiency (79% for **3m**), but 6-chloro diminished the yield of **3n** to 65%. The 3-diazoindolin-2-imine substrate bearing 7-methoxy on the benzo ring also efficiently reacted with **1a** to give the target product **7o** (72%). When 3-diazoindoline-2-imines were replaced by diazoarylacetates, the diazo compounds were decomposed immediately. It was found that the 3-, 4-, and 2-substituents, that is, methoxy, methyl, and fluoro groups, on the aroyl moieties of enaminothiones **1** exhibited no obvious steric and electronic effects, and the corresponding annulation products **3p**−**3u** were formed in 71−80% yields. Only in the case of bearing a 4-bromobenzoyl group, compound **3v** resulted in 63% yield. Bulky 2-naphthalenyl and 2-furanyl and 2-thienyl-supported enaminothiones also reacted well with **2a** to form the target products **3w**−**3y** (71−74%). Notably, imino groups substituted by allyl, propargyl, *n*-butyl, and phenyl were tolerated in the enaminothiones, efficiently resulting in **3z**−**3z3** (71−82%).

The protocol generality was further investigated by means of the reaction of enaminothiones (**1**) with 3-diazooxindoles (**4**) under the modified reaction conditions in the presence of the 10 mol % CuCN catalyst (see the SI file for details). Similar [4 + 1] annulation efficiently occurred with 3-diazooxindoles in refluxing toluene over a period of 5 h (Table 3). The reactions of *N*-methyl, isopropyl, and benzyl-protected 3-diazooxindoles reacted with **1a** to give the corresponding products **5a** (80%), **5b** (78%), and **5c** (86%), respectively. The gram-scale preparation gave **5c** in 78% yield. It is noteworthy that *N*-unprotected 3-diazooxindole did not react under the same conditions. The substituent effect from 4-positioned chloro was observed, decreasing the yield of product **5d** to 68%. However, the 5-, 6-, and 7-substituents such as methoxy, nitro, iodo, fluoro, and methyl did not exhibit obvious steric and/or

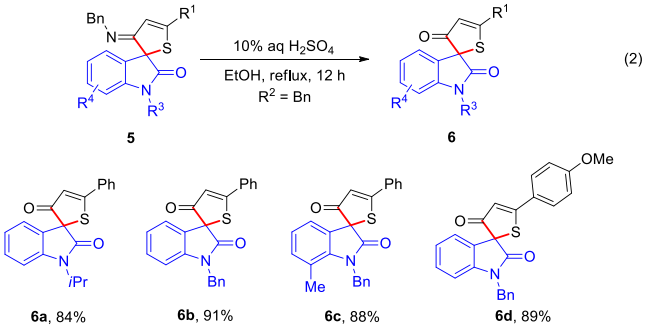
https://doi.org/10.1021/acs.joc.2c00137
J. Org. Chem. 2022, 87, 4424−4437

electronic effects on the reaction efficiency, and the desired products **5e**−**5i** were formed in 79−81% yields. Substituted *N*-benzyl enaminothiones also efficiently underwent the [4 + 1] annulation with *N*-benzyl-3-diazo-oxindole (**4c**), and the corresponding target products **5j**−**5n** could be accessed in 75−85% yields when the substituents on the aroyl moieties of **1** are methyl, methoxy, bromo, and trifluoromethyl. 2-Furanyl-functionalized enaminothione underwent the same type of annulation to generate **5o** (76%), demonstrating a good diversity of the present synthetic method. It should be noted that the molecular structures of the [4 + 1] annulation products of types **3** and **5** were further verified by the X-ray single-crystal structure determination of compound **5a** (see the SI). 3-Diazoindolin-2-imines (**2**) can exhibit a higher reactivity than their corresponding 3-diazooxindoles (**4**), which was exemplified by the competition reactions of **2g** and **4c** with enaminothione **1a** (eq 1). Under the stated conditions using a mixture of 5 mol % $Cu(MeCN)_4BF_4$ and 5 mol % CuCN catalysts, a 2:1 molar ratio mixture of **3g** and **5c** was obtained.



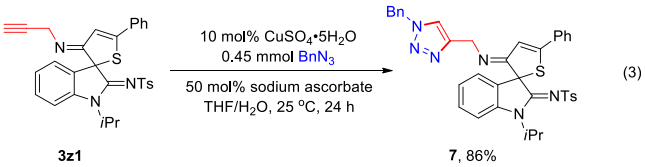
(1)

To demonstrate the practicality of the synthetic protocol, some spiroindoline-dihydrothiophenes **3** and **5** were subjected to the hydrolysis and click reaction conditions, respectively. In the presence of 10% aqueous H_2SO_4 in refluxing ethanol, compounds **3** usually gave a mixture of inseparable unidentified products due to the existence of two imino groups in the substrates. Fortunately, spiroindoline-dihydrothiophenes **5** could be efficiently transformed into the corresponding ketones *via* hydrolysis of the imino group. Thus, spirocyclic indolin-3,2′-thiophen-2,3′-diones (**6a**−**d**) were obtained in 84−91% yields (eq 2). Propargyl-bearing



(2)

spirocycle **3z1** was amenable in copper-catalyzed azide−alkyne cycloaddition to react with (azidomethyl)benzene, giving the corresponding triazole product **7** in 86% yield (eq 3). These transformations have been shown the potential application of the [4 + 1] annulation products for organic synthesis and drug development.Then, control experiments were performed to gain insights into the reaction mechanism (Scheme 2). The addition of a radical scavenger, i.e., 2,2,6,6-tetramethyl-1-



(3)

piperidinyloxy (TEMPO) or 2,6-di-*tert*-butyl-4-methylphenol (BHT), to the reaction of **1a** and **2a** only slightly reduced the yield of **3a** (73−78%), suggesting that the reaction does not proceed through a radical pathway (Scheme 2a). In the case of using an alkylthio-functionalized enaminone substrate, that is, *α*-oxo ketene *N*,*S*-acetal **8**, the corresponding spirocyclic product **3z4** could not be detected (Scheme 2b), which unambiguously demonstrates that a thioxo sulfur atom in **1** is crucial for the investigated [4 + 1] annulation, and the ready formation of an ene-thiol intermediate may play a key role during the process. To verify the role of the terminal olefinic C═C bond-attached alkylthio functionality, terminal methoxy and methyl-functionalized enaminothiones **9** and **10** were treated with **2a** under the standard conditions, respectively. In the case of using methoxy-functionalized enaminothione **9**, the target product **3a** was obtained in 52% yield (Scheme 2c), while no reaction occurred to form the desired product **3z5** in the case of using methyl-functionalized enaminothione **10** (Scheme 2d). These results have shown that a terminal olefinic C═C bond-attached alkylthio functionality in enaminothiones **1** is also crucial as both an effective activating and leaving group for the annulation process.

A plausible mechanism is proposed in Scheme 3. Initially, the interaction of the Cu(I) catalyst with diazo compound **2** or **4** generates Cu(I) metal carbene intermediate **A**. Activation of enaminothione **1** may occur through coordination to the Cu(I) metal center, resulting in complex species **B**. Tautomerism of enaminothione **1** leads to vinyl thiol complex **C**. Subsequent transmetalation gives Cu(I) species **D** followed by a formal carbene insertion into the S−H bond, forming intermediate Cu(I) adduct **E** and regenerating the catalytically active Cu(I) species. Annulation then occurred to produce the target product **3** or **5** with the release of one molecule of methanethiol.

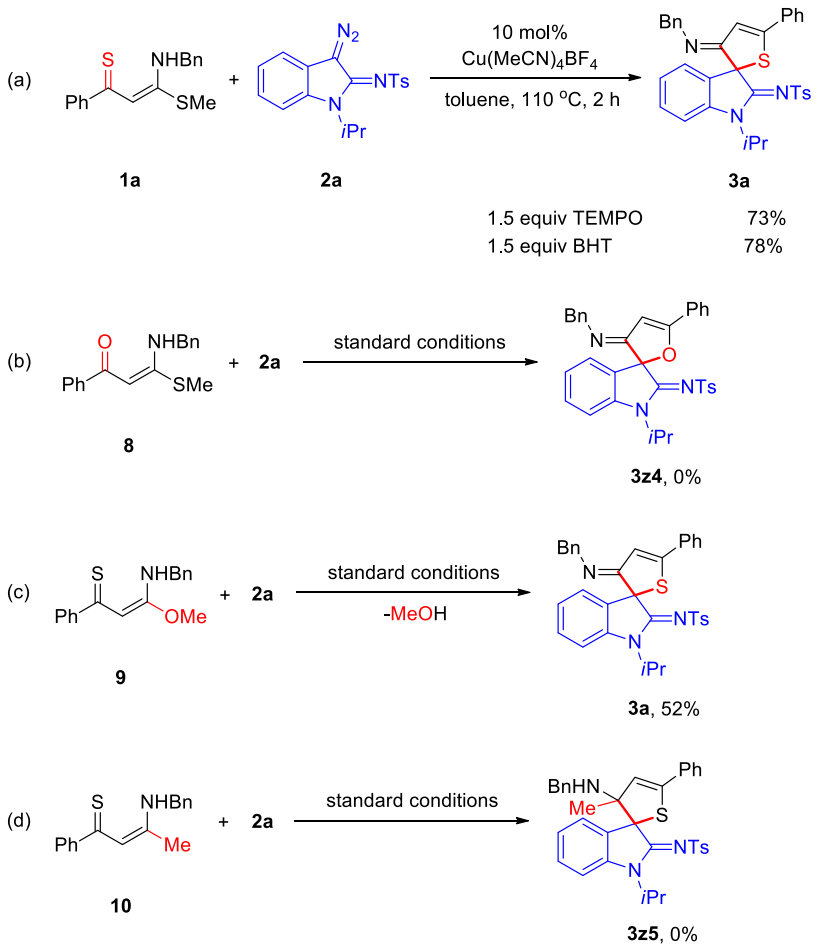
In summary, a concise copper(I)-catalyzed [4 + 1] annulation of alkylthio-functionalized enaminothiones with 3-indoline-based diazo compounds has been successfully developed to access spiroindoline-fused *S*-heterocycles. The present protocol can be efficiently applied with manipulation simplicity and broad substrate scopes. Both 3-diazoindolin-2-imines and 3-diazooxindoles are suitable for the synthesis of spiro *S*-heterocyclic compounds.

■ EXPERIMENTAL SECTION

General Considerations. The solvents were dried and distilled prior to use by the literature methods. ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded on a 400 MHz spectrometer, and all chemical shift values refer to $CDCl_3$ (δ (^1H), 7.26 ppm; δ (^{13}C), 77.16 ppm). For reactions that require heating, an oil bath was used as the heat source. High-resolution mass spectra were measured on a Waters GC-TOF CA156 mass spectrometer. All of the melting points were measured and uncorrected. X-ray crystallographic analysis was achieved by the Analysis Center, Dalian Institute of Chemical Physics, Chinese Academy of Sciences. Analytical TLC plates were viewed by UV light (254 nm). Column chromatographic purifications were performed on SDZF silica gel 160. The starting chemical reagents were purchased from commercial sources and used as received unless otherwise

https://doi.org/10.1021/acs.joc.2c00137
J. Org. Chem. 2022, 87, 4424−4437

Scheme 2. Mechanistic Investigation



indicated. Known compounds, **1a−1o**,[22] **2a−c**,[15c] **2e−2g**,[15c] **4a−4i**,[9] and **8−10**,[22] were prepared as reported, and their spectroscopic features are in good agreement with those reported in the literature.

*Typical Procedure for the Preparation of 2: The Synthesis of (Z)-N-(3-diazo-1-isopropylindolin-2-ylidene)-4-methylbenzenesulfonamide (**2a**).* To an oven-dried 50 mL Schlenk tube equipped with a magnetic stirring bar were sequentially added indole (0.75 mmol), 4-methylbenzenesulfonylazide (1.5 mmol), and DMSO (2 mL). The reaction mixture was stirred at 50 °C for 12 h. Then, the reaction was quenched with H_2O (20 mL) and extracted with CH_2Cl_2 (3 × 45 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The crude product was purified by silica gel column chromatography (eluent: petroleum ether (60−90 °C)/ethyl acetate = 3:1) to afford **2a** as an orange solid (141 mg, 53%).

*(Z)-N-(3-Diazo-1-propylindolin-2-ylidene)-4-methylbenzenesulfonamide (**2d**).* Following the general procedure, compound **2d** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 10:1, v/v). 10 mmol scale, 1.60 g, 45% yield, orange solid, m.p.: 137−138 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 8.3 Hz, 2H), 7.33−7.14 (m, 3H), 7.08 (d, J = 7.9 Hz, 1H), 4.06−3.78 (m, 2H), 2.40 (s, 3H), 1.77−1.66 (m, 2H), 0.90 (t, J = 7.4 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 155.1, 142.4, 140.4, 133.9, 129.5, 126.3, 125.9, 123.0, 119.2, 117.0, 110.1, 44.3, 21.6, 21.2, 11.5. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{18}H_{19}N_4O_2S$: 355.1229; found: 355.1232.

*(Z)-N-(3-Diazo-1-isopropy-4-methylindolin-2-ylidene)-4-methylbenzenesulfonamide (**2h**).* Following the general procedure, compound **2h** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 5 mmol scale, 630 mg, 34% yield, orange solid, m.p.: 182−183 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88−7.86 (m, 2H), 7.28 (d, J = 8.0 Hz, 2H), 7.12 (d, J = 4.7 Hz, 2H), 6.91−6.85 (m, 1H), 4.99 (m, 1H), 2.46 (s, 3H), 2.41 (s, 3H), 1.47 (s, 3H), 1.46 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 156.0, 142.3, 140.8, 132.6, 129.5, 129.4, 126.3, 125.8, 124.7, 116.6, 109.8, 46.7, 21.6, 19.7, 17.4. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{19}H_{21}N_4O_2S$: 369.1385; found: 369.1388.

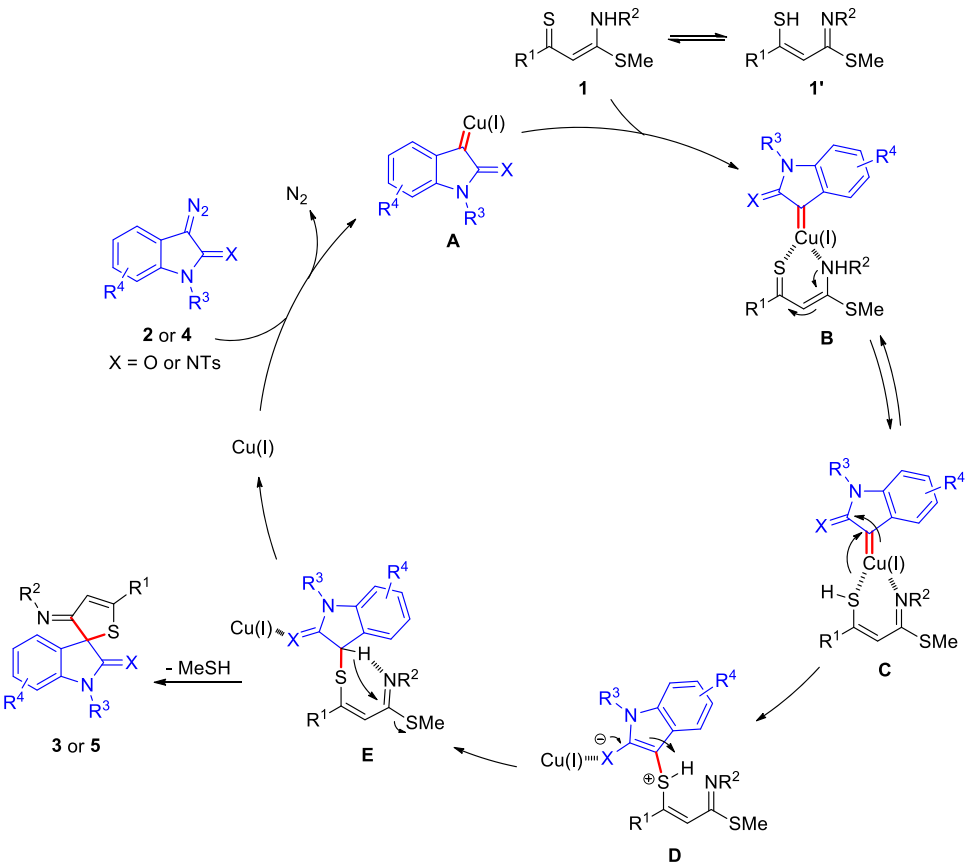
*(Z)-N-(3-Diazo-5-fluoro-1-isopropylindolin-2-ylidene)-4-methylbenzenesulfonamide (**2i**).* Following the general procedure, compound **2i** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 5 mmol scale, 616 mg, 33% yield, orange solid, m.p.: 167−168 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 8.2 Hz, 2H), 7.29 (d, J = 8.1 Hz, 2H), 7.19 (m, 1H), 6.99−6.91 (m, 2H), 5.13−4.95 (m, 1H), 2.42 (s, 3H), 1.48 (s, 3H), 1.46 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.2 (d, $J_{C\text{-}F}$ = 241.8 Hz), 154.7, 142.6, 140.3, 129.5, 128.9, 126.3, 121.2 (d, $J_{C\text{-}F}$ = 10.5 Hz), 112.7 (d, $J_{C\text{-}F}$ = 24.2 Hz), 112.5 (d, $J_{C\text{-}F}$ = 8.9 Hz), 104.5 (d, $J_{C\text{-}F}$ = 27.0 Hz), 46.8, 21.6, 19.7. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{18}H_{18}FN_4O_2S$: 373.1134; found: 373.1129.

*(Z)-N-(5-Chloro-3-diazo-1-isopropylindolin-2-ylidene)-4-methylbenzenesulfonamide (**2j**).* Following the general procedure, compound **2j** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 5 mmol scale, 661 mg, 34% yield, orange solid, m.p.: 190−191 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 8.3 Hz, 2H), 7.21−7.16 (m, 3H), 5.14−4.79 (m, 1H), 2.41 (s, 3H), 1.47 (s, 3H), 1.45 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 154.6, 142.6, 140.2, 131.3, 129.5, 128.4, 126.3, 125.7, 121.3, 117.0, 112.5, 46.9, 21.6, 19.7. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{18}H_{18}ClN_4O_2S$: 389.0839; found: 389.0843.

*(Z)-N-(5-Methyl-carboxylate-3-diazo-1-isopropylindolin-2-ylidene)-4-methylbenzenesul-fonamide (**2k**).* Following the general procedure, compound **2k** was obtained by column chromatography

https://doi.org/10.1021/acs.joc.2c00137
J. Org. Chem. 2022, 87, 4424−4437

Scheme 3. Proposed Mechanism



on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 5 mmol scale, 929 mg, 45% yield, yellow solid, m.p.: 179−180 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.5 Hz, 1H), 7.91 (s, 1H), 7.86 (d, J = 7.7 Hz, 2H), 7.33−7.26 (m, 3H), 5.08−4.96 (m, 1H), 3.93 (s, 3H), 2.41 (s, 3H), 1.50 (s, 3H), 1.48 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.5, 155.2, 142.8, 140.0, 136.2, 129.5, 127.6, 126.4, 124.6, 119.8, 118.3, 111.1, 52.4, 47.0, 21.6, 19.8. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{20}H_{21}N_4O_4S$: 413.1284; found: 413.1291.

*(Z)-N-(3-diazo-1-isopropy-5-methylindolin-2-ylidene)-4-methylbenzenesulfonamide (**2l**).* Following the general procedure, compound **2l** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 5 mmol scale, 554 mg, 30% yield, orange solid, m.p.: 170−171 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 8.1 Hz, 2H), 7.16 (d, J = 8.2 Hz, 1H), 7.07−6.99 (m, 2H), 5.11−4.94 (m, 1H), 2.41 (s, 3H), 2.40 (s, 3H), 1.48 (s, 3H), 1.46 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 154.7, 142.4, 140.6, 132.6, 130.6, 129.4, 126.5, 126.3, 119.8, 117.5, 111.7, 46.6, 21.6, 21.2, 19.8. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{19}H_{21}N_4O_2S$: 369.1385; found: 369.1385.

*(Z)-N-(3-Diazo-6-fluoro-1-isopropylindolin-2-ylidene)-4-methylbenzenesulfonamide (**2m**).* Following the general procedure, compound **2m** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 5 mmol scale, 522 mg, 28% yield, orange solid, m.p.: 154−155 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 8.3 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 7.14 (m, 5.0 Hz, 1H), 7.02 (m, 1H), 6.91 (m, 1H), 5.07−4.92 (m, 1H), 2.42 (s, 3H), 1.48 (s, 3H), 1.46 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.5 (d, $J_{C\text{-}F}$ = 243.2 Hz), 155.6, 142.6, 140.2, 133.5 (d, $J_{C\text{-}F}$ = 11.8 Hz), 129.5, 126.4, 117.8 (d, $J_{C\text{-}F}$ = 9.8 Hz), 114.9 (d, $J_{C\text{-}F}$ = 1.9 Hz), 109.8 (d, $J_{C\text{-}F}$ = 23.9 Hz), 100.3 (d, $J_{C\text{-}F}$ = 29.0 Hz), 46.9, 21.6, 19.6. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{18}H_{18}FN_4O_2S$: 373.1134; found: 373.1127.

*(Z)-N-(6-Chloro-3-diazo-1-isopropylindolin-2-ylidene)-4-methylbenzenesulfonamide (**2n**).* Following the general procedure, compound **2n** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 5 mmol scale, 564 mg, 29% yield, orange solid, m.p.: 157−158 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 8.2 Hz, 2H), 7.29 (d, J = 7.9 Hz, 2H), 7.28−7.24 (m, 1H), 7.19−7.11 (m, 2H), 5.07−4.91 (m, 1H), 2.42 (s, 3H), 1.48 (s, 3H), 1.46 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 155.1, 142.7, 140.1, 133.6, 131.5, 129.5, 126.4, 122.8, 118.0, 117.7, 112.1, 46.9, 21.6, 19.7. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{18}H_{18}ClN_4O_2S$: 389.0839; found: 389.0840.

*(Z)-N-(3-Diazo-1-isopropyl-7-methoxyindolin-2-ylidene)-4-methylbenzenesulfonamide (**2o**).* Following the general procedure, compound **2o** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 5 mmol scale, 526 mg, 27% yield, orange solid, m.p.: 154−155 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.1 Hz, 2H), 7.29 (d, J = 7.9 Hz, 2H), 7.20−7.07 (m, 1H), 6.88−6.74 (m, 2H), 5.84−5.12 (m, 1H), 3.93 (s, 3H), 2.41 (s, 3H), 1.49 (s, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 154.6, 146.5, 142.2, 140.6, 129.3, 126.1, 123.7, 122.0, 109.4, 109.0, 64.9, 55.7, 50.8, 46.9, 21.5, 20.6, 19.8. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{19}H_{21}N_4O_3S$: 385.1334; found: 385.1333.

*Typical Procedure for the Preparation of 3: The Synthesis of N-(3′-(Benzylimino)-1-methyl-5′-phenyl-3′H-spiro[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3b**).* A mixture of **1a** (90 mg, 0.3 mmol), **2b** (147 mg, 0.45 mmol), and Cu(MeCN)$_4$BF$_4$ (9.4 mg, 0.03 mmol) in 2 mL of toluene was vigorously stirred at 110 °C for 2 h under a nitrogen atmosphere. After cooling to ambient temperature, all of the volatiles were evaporated under reduced pressure. The resultant residue was purified by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/ethyl acetate = 10:1, v/v) to afford product **3b** (125 mg, 76%).

*N-(3′-(Benzylimino)-1-isopropyl-5′-phenyl-3′H-spiro[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3a**).* Following the general procedure, compound **3a** was obtained by column

https://doi.org/10.1021/acs.joc.2c00137
J. Org. Chem. 2022, 87, 4424−4437

chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 146 mg, 84% yield, orange solid, m.p.: 161−162 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81−7.58 (m, 4H), 7.45 (s, 3H), 7.37−6.98 (m, 11H), 6.88 (s, 1H), 4.97−4.40 (m, 3H), 2.34 (s, 3H), 1.46 (m, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.6, 165.0, 161.5, 141.8, 141.0, 140.5, 140.4, 134.8, 133.1, 131.0, 129.0, 128.2, 127.4, 127.0, 126.5, 126.4, 123.8, 123.0, 111.4, 108.8, 65.9, 57.0, 47.1, 21.6, 19.2, 19.2. HRMS (ESI-TOF) *m/z*: [M + H]$^+$ calcd for $C_{34}H_{32}N_3O_2S_2$: 578.1936; found: 578.1938.

*N-(3′-(Benzylimino)-1-methyl-5′-phenyl-3′H-spiro[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3b**).* Following the general procedure, compound **3b** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 10:1, v/v). 125 mg, 76% yield, orange solid, m.p.: 182−183 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69−7.50 (m, 4H), 7.36−7.23 (m, 3H), 7.20−6.90 (m, 10H), 6.83−6.70 (m, 2H), 4.59 (m, 2H), 3.19 (s, 3H), 2.24 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 174.2, 165.3, 161.5, 142.1, 141.6, 140.6, 139.9, 134.1, 132.9, 131.0, 129.4, 129.0, 128.9, 128.2, 127.4, 126.9, 126.6, 126.5, 124.3, 122.6, 109.8, 109.0, 65.8, 57.4, 29.6, 21.5. HRMS (ESI-TOF) *m/z*: [M + H]$^+$ calcd for $C_{32}H_{28}N_3O_2S_2$: 550.1623; found: 550.1635.

*N-(3′-(Benzylimino)-1-ethyl-5′-phenyl-3′H-spiro[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3c**).* Following the general procedure, compound **3c** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 137 mg, 81% yield, orange solid, m.p.: 179−180 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80−7.68 (m, 4H), 7.50−7.41 (m, 3H), 7.36−7.25 (m, 2H), 7.24−7.04 (m, 8H), 6.98−6.89 (m, 2H), 4.70 (m, 2H), 4.04−3.77 (m, 2H), 2.35 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.8, 164.8, 161.4, 141.9, 140.8, 140.8, 140.2, 134.4, 133.0, 131.0, 129.3, 129.2, 129.0, 128.2, 127.4, 127.0, 126.5, 126.4, 124.1, 122.8, 109.7, 109.0, 65.8, 57.1, 37.8, 21.5, 12.1. HRMS (ESI-TOF) *m/z*: [M + H]$^+$ calcd for $C_{33}H_{30}N_3O_2S_2$: 564.1779; found: 564.1772.

*N-(3′-(Benzylimino)-5′-phenyl-1-propyl-3′H-spiro[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3d**).* Following the general procedure, compound **3d** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 135 mg, 78% yield, orange solid, m.p.: 165−166 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84−7.66 (m, 4H), 7.54−7.42 (m, 3H), 7.37−7.27 (m, 2H), 7.26−7.15 (m, 5H), 7.14−7.05 (m, 3H), 7.01−6.91 (m, 2H), 4.86−4.50 (m, 2H), 4.06−3.62 (m, 2H), 2.35 (s, 3H), 1.70 (m, 2H), 0.86 (t, *J* = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.7, 165.3, 161.5, 141.9, 141.3, 140.7, 140.2, 134.4, 133.1, 131.0, 129.3, 129.0, 128.1, 127.5, 127.0, 126.6, 126.4, 124.1, 122.8, 109.9, 109.0, 65.9, 57.3, 44.4, 21.6, 20.4, 11.4. HRMS (ESI-TOF) *m/z*: [M + H]$^+$ calcd for $C_{34}H_{32}N_3O_2S_2$: 578.1936; found: 578.1932.

*N-(3′-(Benzylimino)-1-butyl-5′-phenyl-3′H-spiro[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3e**).* Following the general procedure, compound **3e** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 130 mg, 73% yield, orange solid, m.p.: 172−173 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84−7.65 (m, 4H), 7.52−7.39 (m, 3H), 7.34−7.15 (m, 7H), 7.13−7.02 (m, 3H), 7.00−6.87 (m, 2H), 4.71 (dd, *J* = 80.5, 16.2 Hz, 2H), 4.07−3.63 (m, 2H), 2.35 (s, 3H), 1.63 (dd, *J* = 14.3, 7.1 Hz, 2H), 1.42−1.14 (m, 2H), 0.78 (t, *J* = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.5, 165.0, 161.4, 141.8, 141.1, 140.6, 140.2, 134.3, 133.0, 131.0, 129.2, 128.9, 128.8, 128.1, 127.5, 126.9, 126.5, 126.4, 124.0, 122.7, 109.8, 108.9, 65.7, 57.2, 42.5, 29.0, 21.5, 19.9, 13.7. HRMS (ESI-TOF) *m/z*: [M + H]$^+$ calcd for $C_{35}H_{34}N_3O_2S_2$: 592.2092; found: 592.2067.

*N-(1-Allyl-3′-(benzylimino)-5′-phenyl-3′H-spiro[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3f**).* Following the general procedure, compound **3f** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 133 mg, 77% yield, orange solid, m.p.: 154−155 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78−7.64 (m, 4H), 7.51−7.41 (m, 3H), 7.33−7.23 (m, 2H), 7.21−7.03 (m, 8H), 6.95−6.84 (m, 2H), 5.85−5.68 (m, 1H), 5.31 (d, *J* = 17.2 Hz, 1H), 5.10 (d, *J* = 10.4 Hz, 1H), 4.76 (d, *J* = 16.1 Hz, 1H), 4.68−4.54 (m, 2H), 4.34 (d, *J* = 16.4 Hz, 1H), 2.35 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.7, 165.3, 161.6, 142.0, 140.9, 140.7, 140.2, 134.3, 133.1, 131.1, 129.5, 129.3, 129.0, 128.2, 127.6, 127.0, 126.6, 126.5, 124.2, 122.8, 118.1, 110.3, 108.9, 65.9, 57.3, 45.0, 21.6. HRMS (ESI-TOF) *m/z*: [M + H]$^+$ calcd for $C_{34}H_{30}N_3O_2S_2$: 576.1779; found: 576.1775.

*N-(1-Benzyl-3′-(benzylimino)-5′-phenyl-3′H-spiro[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3g**).* Following the general procedure, compound **3g** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 145 mg, 77% yield, orange solid, m.p.: 173−174 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79−7.73 (m, 2H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.51−7.44 (m, 3H), 7.31 (d, *J* = 7.4 Hz, 3H), 7.20 (m, 7H), 7.09 (m, 3H), 7.02 (m, 2H), 6.96 (s, 1H), 6.79 (d, *J* = 7.8 Hz, 1H), 5.42 (d, *J* = 15.7 Hz, 1H), 4.86−4.68 (m, 2H), 4.59 (d, *J* = 16.3 Hz, 1H), 2.32 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.5, 165.8, 161.6, 142.0, 140.8, 140.5, 140.3, 134.4, 134.3, 133.1, 131.1, 129.3, 129.0, 129.0, 128.8, 128.2, 127.8, 127.6, 127.3, 127.0, 126.5, 124.3, 122.8, 110.5, 108.9, 65.9, 57.5, 46.3, 21.5. HRMS (ESI-TOF) *m/z*: [M + H]$^+$ calcd for $C_{38}H_{32}N_3O_2S_2$: 626.1936; found: 626.1932.

*N-(3′-(Benzylimino)-1-isopropyl-4-methyl-5′-phenyl-3′H-spiro-[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3h**).* Following the general procedure, compound **3h** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 96 mg, 54% yield, orange solid, m.p.: 172−173 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77−7.65 (m, 4H), 7.50−7.41 (m, 3H), 7.25−7.15 (m, 6H), 7.09 (d, *J* = 7.9 Hz, 2H), 7.02 (s, 1H), 6.97 (d, *J* = 7.9 Hz, 1H), 6.88 (d, *J* = 7.7 Hz, 1H), 4.91−4.71 (m, 2H), 4.62 (d, *J* = 16.1 Hz, 1H), 2.34 (s, 3H), 2.20 (s, 3H), 1.47 (m, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 172.3, 164.5, 160.4, 141.7, 141.6, 141.4, 140.5, 135.8, 133.2, 131.4, 130.9, 129.0, 129.0, 128.9, 128.2, 127.5, 126.9, 126.5, 126.4, 126.3, 111.7, 109.0, 66.6, 57.5, 47.3, 21.6, 19.1, 19.1, 17.8. HRMS (ESI-TOF) *m/z*: [M + H]$^+$ calcd for $C_{35}H_{34}N_3O_2S_2$: 592.2092; found: 592.2104.

*N-(3′-(Benzylimino)-1-isopropyl-5-methyl-5′-phenyl-3′H-spiro-[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3i**).* Following the general procedure, compound **3i** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 148 mg, 83% yield, orange solid, m.p.: 179−180 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83−7.76 (m, 2H), 7.73 (d, *J* = 8.0 Hz, 2H), 7.52−7.43 (m, 3H), 7.26−7.18 (m, 5H), 7.17−7.01 (m, 5H), 6.95 (s, 1H), 4.94−4.76 (m, 2H), 4.63 (d, *J* = 16.5 Hz, 1H), 2.35 (s, 3H), 2.31 (s, 3H), 1.56−1.43 (m, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.6, 164.7, 161.2, 141.6, 141.0, 140.4, 137.8, 134.7, 133.5, 133.0, 130.9, 129.4, 128.8, 128.0, 127.3, 126.9, 126.3, 126.2, 123.4, 111.1, 108.7, 65.7, 56.8, 46.9, 21.4, 20.9, 19.1, 19.0. HRMS (ESI-TOF) *m/z*: [M + H]$^+$ calcd for $C_{35}H_{34}N_3O_2S_2$: 592.2092; found: 592.2096.

*N-(3′-(Benzylimino)-5-fluoro-1-isopropyl-5′-phenyl-3′H-spiro-[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3j**).* Following the general procedure, compound **3j** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 147 mg, 82% yield, orange solid, m.p.: 215−216 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79−7.64 (m, 4H), 7.51−7.38 (m, 3H), 7.25−7.14 (m, 5H), 7.13−6.95 (m, 5H), 6.92 (s, 1H), 4.91−4.70 (m, 2H), 4.60 (d, *J* = 16.4 Hz, 1H), 2.35 (s, 3H), 1.58−1.34 (m, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.1, 164.8, 161.1 (d, J_{C-F} = 45.2 Hz), 158.4, 141.9, 140.8, 140.2, 136.4, 136.3, 132.8, 131.1, 129.0, 128.1, 127.4, 126.9, 126.4, 126.4, 115.5 (d, J_{C-F} =23.8 Hz), 112.1 (d, J_{C-F} = 7.8 Hz), 110.8 (d, J_{C-F} = 25.6 Hz), 108.7, 65.6, 57.0, 47.1, 21.5, 19.0, 19.0. HRMS (ESI-TOF) *m/z*: [M + H]$^+$ calcd for $C_{34}H_{31}FN_3O_2S_2$: 596.1842; found: 596.1849.

*N-(3′-(Benzylimino)-5-chloro-1-isopropyl-5′-phenyl-3′H-spiro-[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3k**).* Following the general procedure, compound **3k** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 152 mg, 83% yield, orange solid, m.p.: 223−224 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83−7.73 (m, 2H), 7.68 (d, *J* = 7.7 Hz, 2H), 7.55−7.43 (m, 3H), 7.36−7.18 (m, 7H), 7.15−7.00 (m, 3H), 6.93 (s, 1H), 4.91−4.72 (m, 2H), 4.61 (d, *J* = 16.4 Hz, 1H), 2.37 (s, 3H), 1.52−1.41 (m, 6H). $^{13}C\{^1H\}$ NMR (100

https://doi.org/10.1021/acs.joc.2c00137
J. Org. Chem. 2022, 87, 4424−4437

MHz, $CDCl_3$) δ 173.1, 164.6, 161.4, 142.0, 140.6, 140.2, 139.0, 136.4, 132.8, 131.1, 129.1, 129.0, 129.0, 128.2, 127.4, 127.0, 126.4, 123.3, 112.3, 108.7, 65.4, 57.1, 47.2, 21.5, 19.1, 19.0. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{34}H_{31}ClN_3O_2S_2$: 612.1546; found: 612.1537.

*Methyl-3′-(benzylimino)-1-isopropyl-5′-phenyl-2-(tosylimino)-3′H-spiro[indoline-3,2′-thiophene]-5-carboxylate (**3l**).* Following the general procedure, compound **3l** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 158 mg, 83% yield, orange solid, m.p.: 180−181 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.2 Hz, 1H), 8.01 (s, 1H), 7.83−7.74 (m, 2H), 7.69 (d, *J* = 7.9 Hz, 2H), 7.53−7.41 (m, 3H), 7.25−7.13 (m, 6H), 7.09 (d, *J* = 7.9 Hz, 2H), 6.94 (s, 1H), 4.92−4.69 (m, 2H), 4.58 (d, *J* = 16.5 Hz, 1H), 3.86 (s, 3H), 2.35 (s, 3H), 1.60−1.37 (m, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.2, 166.3, 165.3, 161.3, 144.6, 142.1, 140.4, 140.2, 134.8, 132.8, 131.4, 131.0, 129.0, 128.9, 128.1, 127.4, 127.0, 126.4, 126.4, 125.5, 124.2, 110.8, 108.8, 65.2, 57.1, 52.2, 47.3, 21.5, 19.0, 19.0. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{36}H_{34}N_3O_4S_2$: 636.1991; found: 636.1996.

*N-(3′-(Benzylimino)-6-fluoro-1-isopropyl-5′-phenyl-3′H-spiro-[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3m**).* Following the general procedure, compound **3m** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 141 mg, 79% yield, orange solid, m.p.: 197−198 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78−7.70 (m, 2H), 7.68 (d, *J* = 8.2 Hz, 2H), 7.49−7.41 (m, 3H), 7.25−7.16 (m, 6H), 7.10 (d, *J* = 8.1 Hz, 2H), 6.91 (s, 1H), 6.85 (m, 1H), 6.78−6.71 (m, 1H), 4.86−4.71 (m, 2H), 4.59 (d, *J* = 16.4 Hz, 1H), 2.36 (s, 3H), 1.50−1.42 (m, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.4, 165.4, 164.4, 161.9, 161.3, 142.0, 141.81 (d, J_{C-F} = 11.9 Hz), 140.42 (d, J_{C-F} = 31.7 Hz), 132.9, 131.0, 130.1 (d, J_{C-F} = 2.5 Hz), 129.0, 128.9, 128.1, 127.4, 126.9, 126.4, 124.0, 123.9, 110.0 (d, J_{C-F} = 22.8 Hz), 108.6, 100.0 (d, J_{C-F} = 28.6 Hz), 65.3, 57.0, 47.2, 21.5, 19.0, 19.0. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{34}H_{31}FN_3O_2S_2$: 596.1842; found: 596.1833.

*N-(3′-(Benzylimino)-6-chloro-1-isopropyl-5′-phenyl-3′H-spiro-[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3n**).* Following the general procedure, compound **3n** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 119 mg, 65% yield, orange solid, m.p.: 203−204 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76−7.68 (m, 2H), 7.65 (d, *J* = 8.1 Hz, 2H), 7.51−7.41 (m, 3H), 7.24−7.15 (m, 6H), 7.13−7.05 (m, 3H), 7.02 (dd, *J* = 8.1, 1.5 Hz, 1H), 6.90 (s, 1H), 4.83−4.71 (m, 2H), 4.58 (d, *J* = 16.4 Hz, 1H), 2.35 (s, 3H), 1.46 (m, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.2, 165.1, 161.4, 142.0, 141.7, 140.6, 140.3, 134.6, 133.1, 132.9, 131.1, 129.0, 129.0, 128.2, 127.4, 127.0, 126.5, 123.8, 123.6, 111.8, 108.7, 65.3, 57.1, 47.2, 21.6, 19.0, 19.0. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{34}H_{31}ClN_3O_2S_2$: 612.1546; found: 612.1552.

*N-(3′-(Benzylimino)-1-isopropyl-7-methoxy-5′-phenyl-3′H-spiro-[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3o**).* Following the general procedure, compound **3o** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 131 mg, 72% yield, orange solid, m.p.: 200−201 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80−7.70 (m, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.53−7.40 (m, 1H), 7.20 (d, J = 7.1 Hz, 2H), 7.08 (d, *J* = 7.9 Hz, 1H), 7.02 (t, *J* = 7.9 Hz, 1H), 6.96−6.80 (m, 1H), 5.32 (dt, *J* = 13.6, 6.7 Hz, 1H), 4.80 (d, *J* = 16.4 Hz, 1H), 4.59 (d, *J* = 16.4 Hz, 1H), 3.87 (s, 1H), 2.35 (s, 1H), 1.51 (d, *J* = 6.6 Hz, 1H), 1.38 (d, *J* = 6.5 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.7, 164.9, 161.3, 145.6, 141.6, 141.1, 140.5, 133.2, 130.9, 128.9, 128.1, 127.5, 127.0, 126.4, 126.4, 124.9, 115.4, 113.1, 108.8, 66.2, 57.1, 55.9, 49.9, 21.6, 19.6. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{35}H_{34}N_3O_3S_2$: 608.2042; found: 608.2061.

*N-(3′-(Benzylimino)-1-isopropyl-5′-(3-methoxyphenyl)-3′H-spiro[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3p**).* Following the general procedure, compound **3p** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 140 mg, 77% yield, orange solid, m.p.: 185−186 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.2 Hz, 2H), 7.39 (m, 2H), 7.35 (m, 1H), 7.30 (m, 2H), 7.27−7.19 (m, 5H), 7.17−7.07 (m, 4H), 7.03 (m, 1H), 6.94 (s, 1H), 4.95−4.77 (m, 2H), 4.63 (d, *J* = 16.5 Hz, 1H), 3.88 (s, 3H), 2.38 (s, 3H), 1.59−1.42 (m, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.4, 164.8, 161.2, 159.8, 141.7, 140.9, 140.3, 140.3, 134.6, 134.3, 129.9, 128.9, 128.9, 128.0, 127.3, 126.3, 126.3, 123.7, 122.8, 119.4, 116.8, 112.0, 111.3, 109.0, 65.7, 56.9, 55.4, 47.0, 21.4, 19.0, 19.0. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{35}H_{34}N_3O_3S_2$: 608.2042; found: 608.2041.

*N-(3′-(Benzylimino)-1-isopropyl-5′-(p-tolyl)-3′H-spiro[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3q**).* Following the general procedure, compound **3q** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 137 mg, 77% yield, orange solid, m.p.: 198−199 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.1 Hz, 2H), 7.63 (d, *J* = 8.1 Hz, 2H), 7.34−7.26 (m, 3H), 7.25 (s, 1H), 7.21−7.14 (m, 5H), 7.12 (d, *J* = 7.9 Hz, 1H), 7.10−7.01 (m, 3H), 6.86 (s, 1H), 4.93−4.71 (m, 2H), 4.57 (d, *J* = 16.5 Hz, 1H), 2.41 (s, 3H), 2.35 (s, 3H), 1.53−1.41 (m, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.7, 165.0, 161.4, 141.8, 141.4, 141.0, 140.5, 140.3, 134.8, 130.3, 129.6, 129.0, 128.1, 127.4, 126.9, 126.4, 126.3, 123.7, 122.9, 111.4, 108.0, 65.8, 56.9, 47.0, 21.6, 21.5, 19.1, 19.1. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{35}H_{34}N_3O_2S_2$: 592.2092; found: 592.2082.

*N-(3′-(Benzylimino)-1-isopropyl-5′-(4-methoxyphenyl)-3′H-spiro[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3r**).* Following the general procedure, compound **3r** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 130 mg, 71% yield, orange solid, m.p.: 197−198 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79−7.63 (m, 4H), 7.35−7.27 (m, 2H), 7.26−7.17 (m, 5H), 7.16−7.03 (m, 4H), 7.03−6.93 (m, 2H), 6.83 (s, 1H), 4.96−4.69 (m, 2H), 4.59 (d, *J* = 16.3 Hz, 1H), 3.87 (s, 3H), 2.40 (s, 3H), 1.63−1.37 (m, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.7, 165.0, 161.8, 160.9, 141.7, 141.0, 140.6, 140.3, 134.9, 128.9, 128.5, 128.1, 127.3, 126.4, 126.3, 125.6, 123.7, 122.9, 114.3, 111.3, 107.1, 65.8, 56.8, 55.5, 47.0, 21.5, 19.1, 19.1. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{35}H_{34}N_3O_3S_2$: 608.2042; found: 608.2044.

*N-(3′-(Benzylimino)-5′-(2-fluorophenyl)-1-isopropyl-3′H-spiro-[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3s**).* Following the general procedure, compound **3s** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 136 mg, 76% yield, orange solid, m.p.: 183−184 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74−7.64 (m, 3H), 7.44−7.36 (m, 1H), 7.34 (m, 1H), 7.29 (m, 1H), 7.24−7.15 (m, 7H), 7.14−7.01 (m, 5H), 4.91−4.73 (m, 2H), 4.63 (d, *J* = 16.5 Hz, 1H), 2.34 (s, 3H), 1.52−1.41 (m, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.8, 164.8, 161.3, 158.8, 154.2, 141.8, 140.8, 140.3, 140.2, 134.5, 132.1 (d, J_{C-F} = 8.9 Hz), 129.6 (d, J_{C-F} = 1.9 Hz), 129.0, 128.9, 128.0, 127.3, 126.3, 126.3, 124.7 (d, J_{C-F} = 3.3 Hz), 123.7, 122.8, 121.1 (d, J_{C-F} = 11.6 Hz), 116.4 (d, J_{C-F} = 22.3 Hz), 112.9 (d, J_{C-F} = 12.1 Hz), 111.3, 64.8, 57.0, 47.0, 21.4, 19.0, 19.0. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{34}H_{31}FN_3O_2S_2$: 596.1842; found: 596.1847.

*N-(3′-(Benzylimino)-5′-(3-fluorophenyl)-1-isopropyl-3′H-spiro-[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3t**).* Following the general procedure, compound **3t** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 143 mg, 80% yield, orange solid, m.p.: 191−192 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.2 Hz, 2H), 7.55 (d, *J* = 7.8 Hz, 1H), 7.50−7.40 (m, 2H), 7.31 (t, *J* = 7.2 Hz, 2H), 7.26−7.06 (m, 10H), 6.93 (s, 1H), 4.94−4.76 (m, 2H), 4.62 (d, *J* = 16.5 Hz, 1H), 2.38 (s, 3H), 1.55−1.44 (m, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.2, 164.7, 164.1, 161.6, 159.8, 141.9, 140.8, 140.3 (d, J_{C-F} = 13.4 Hz), 135.2 (d, J_{C-F} = 7.7 Hz), 134.4, 130.6 (d, J_{C-F} = 8.3 Hz), 129.1, 129.0, 128.1, 127.3, 126.4, 123.8, 122.9, 122.8 (d, J_{C-F} = 2.7 Hz), 117.7 (d, J_{C-F} = 21.4 Hz), 113.8 (d, J_{C-F} = 22.9 Hz), 111.4, 109.7, 65.8, 57.0, 47.0, 21.5, 19.1, 19.0. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{34}H_{31}FN_3O_2S_2$: 596.1842; found: 596.1841.

*N-(3′-(Benzylimino)-5′-(4-fluorophenyl)-1-isopropyl-3′H-spiro-[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3u**).* Following the general procedure, compound **3u** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 141 mg, 79% yield, orange solid, m.p.:

https://doi.org/10.1021/acs.joc.2c00137
J. Org. Chem. 2022, 87, 4424−4437

201−202 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90−7.59 (m, 4H), 7.41−6.96 (m, 13H), 6.83 (s, 1H), 5.01−4.69 (m, 2H), 4.58 (d, *J* = 15.5 Hz, 1H), 2.37 (s, 3H), 1.67−1.40 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 173.4, 165.6, 164.9, 160.2, 141.9, 141.0, 140.5, 134.7, 129.5 (d, J_{C-F} = 3.7 Hz), 129.1 (d, J_{C-F} = 4.4 Hz), 128.2, 127.4, 126.5, 123.8, 123.0, 116.3, 116.0, 111.5, 108.8, 66.1, 57.1, 47.1, 21.6, 19.2. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{34}H_{31}FN_3O_2S_2$: 596.1842; found: 596.1844.

*N-(3′-(Benzylimino)-1-isopropyl-5-methyl-5′-phenyl-3′H-spiro-[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3v**).* Following the general procedure, compound **3v** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 124 mg, 63% yield, orange solid, m.p.: 210−211 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 7.9 Hz, 2H), 7.60−7.53 (m, 4H), 7.33−7.26 (m, 2H), 7.22−7.02 (m, 9H), 6.85 (s, 1H), 4.90−4.68 (m, 2H), 4.55 (d, *J* = 16.4 Hz, 1H), 2.34 (s, 3H), 1.51−1.40 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 173.3, 164.8, 160.0, 141.9, 140.9, 140.4, 140.3, 134.6, 132.2, 132.1, 129.1, 129.0, 128.4, 128.2, 127.4, 126.4, 125.2, 123.8, 123.0, 111.4, 109.2, 66.0, 57.1, 47.1, 21.6, 19.2. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{34}H_{31}BrN_3O_2S_2$: 656.1041; found: 656.1038.

*N-(3′-(Benzylimino)-1-isopropyl-5′-(naphthalen-2-yl)-3′H-spiro-[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3w**).* Following the general procedure, compound **3w** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 134 mg, 71% yield, orange solid, m.p.: 192−193 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.94−7.80 (m, 4H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.60−7.49 (m, 2H), 7.35 (d, *J* = 7.4 Hz, 1H), 7.31−7.26 (m, 1H), 7.25−7.19 (m, 5H), 7.14 (d, *J* = 8.0 Hz, 1H), 7.11−6.99 (m, 4H), 4.95−4.78 (m, 2H), 4.65 (d, *J* = 16.5 Hz, 1H), 2.35 (s, 3H), 1.56−1.42 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 173.5, 165.0, 161.1, 141.8, 141.0, 140.4, 140.3, 134.8, 134.4, 133.0, 130.4, 128.9, 128.8, 128.6, 128.1, 127.8, 127.6, 127.4, 127.2, 126.9, 126.4, 126.3, 123.8, 122.9, 111.4, 109.1, 65.8, 57.0, 47.0, 21.5, 19.1, 19.1. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{38}H_{34}N_3O_2S_2$: 628.2092; found: 628.2100.

*N-(3′-(Benzylimino)-5′-(furan-2-yl)-1-isopropyl-3′H-spiro-[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3x**).* Following the general procedure, compound **3x** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 123 mg, 72% yield, orange solid, m.p.: 188−189 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.2 Hz, 2H), 7.60−7.55 (m, 1H), 7.32 (d, *J* = 7.3 Hz, 1H), 7.30−7.27 (m, 1H), 7.25−7.17 (m, 5H), 7.16−7.04 (m, 4H), 6.87 (s, 1H), 6.85 (d, *J* = 3.4 Hz, 1H), 6.58−6.51 (m, 1H), 4.92−4.81 (m, 1H), 4.77 (d, *J* = 16.5 Hz, 1H), 4.58 (d, *J* = 16.5 Hz, 1H), 2.37 (s, 3H), 1.55−1.43 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 173.1, 164.7, 148.4, 147.8, 144.9, 141.8, 140.9, 140.4, 140.3, 134.7, 129.0, 128.9, 128.0, 127.3, 126.4, 126.3, 123.7, 122.9, 113.0, 112.6, 111.3, 106.8, 65.4, 57.0, 47.0, 21.5, 19.1. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{32}H_{30}N_3O_3S_2$: 568.1729; found: 568.1728.

*N-(3′-(Benzylimino)-1-isopropyl-5′-(thiophen-2-yl)-3′H-spiro-[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3y**).* Following the general procedure, compound **3y** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 130 mg, 74% yield, orange solid, m.p.: 194−195 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.1 Hz, 2H), 7.50−7.43 (m, 2H), 7.34−7.25 (m, 2H), 7.24−7.15 (m, 5H), 7.15−7.02 (m, 5H), 6.74 (s, 1H), 4.91−4.79 (m, 1H), 4.75 (d, *J* = 16.6 Hz, 1H), 4.56 (d, *J* = 16.6 Hz, 1H), 2.35 (s, 3H), 1.56−1.41 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 173.0, 164.8, 153.4, 141.8, 140.9, 140.4, 140.3, 136.2, 134.7, 129.0, 129.0, 129.0, 128.8, 128.3, 128.1, 127.3, 126.4, 126.3, 123.7, 123.0, 111.4, 108.0, 66.0, 57.0, 47.0, 21.5, 19.1, 19.1. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{32}H_{30}N_3O_2S_3$: 584.1500; found: 584.1493.

*N-(3′-(Allylimino)-1-isopropyl-5′-phenyl-3′H-spiro[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3z**).* Following the general procedure, compound **3z** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 130 mg, 82% yield, orange solid, m.p.: 179−180 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.2 Hz, 2H), 7.77−7.69 (m, 2H), 7.51−7.41 (m, 3H), 7.34−7.19 (m, 4H), 7.13 (d, *J* = 8.0 Hz, 1H), 7.06 (dd, *J* = 15.0, 7.8 Hz, 1H), 6.82 (s, 1H), 6.01−5.86 (m, 1H), 5.14−4.96 (m, 2H), 4.93−4.78 (m, 1H), 4.27−4.14 (m, 1H), 4.11−3.99 (m, 1H), 2.41 (s, 3H), 1.57−1.44 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 173.7, 164.9, 160.8, 141.9, 141.1, 140.3, 136.1, 134.8, 133.1, 130.9, 129.0, 129.0, 128.9, 126.9, 126.5, 123.8, 122.9, 114.8, 111.4, 109.0, 65.6, 55.9, 47.0, 21.6, 19.2, 19.1. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{30}H_{30}N_3O_2S_2S$: 528.1779; found: 528.1782.

*N-(1-Isopropyl-5′-phenyl-3′-(prop-2-yn-1-ylimino)-3′H-spiro-[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3z1**).* Following the general procedure, compound **3z1** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 118 mg, 75% yield, orange solid, m.p.: 220−221 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.2 Hz, 2H), 7.71 (dd, *J* = 7.5, 2.0 Hz, 2H), 7.52−7.40 (m, 3H), 7.30−7.19 (m, 4H), 7.10 (d, *J* = 7.9 Hz, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.85 (s, 1H), 4.82 (dt, *J* = 13.7, 6.7 Hz, 1H), 4.33−4.22 (m, 1H), 4.20−4.09 (m, 1H), 2.39 (s, 3H), 2.19 (t, *J* = 2.6 Hz, 1H), 1.54−1.39 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 176.1, 164.4, 162.3, 142.0, 140.9, 140.3, 134.2, 132.9, 131.2, 129.1, 129.1, 129.0, 127.1, 126.6, 124.0, 122.9, 111.5, 109.2, 81.5, 70.9, 65.6, 47.2, 42.2, 21.6, 19.2, 19.2. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{30}H_{28}N_3O_2S_2$: 526.1623; found: 526.1626.

*N-(3′-(Butylimino)-1-isopropyl-5′-phenyl-3′H-spiro[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3z2**).* Following the general procedure, compound **3z2** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 116 mg, 71% yield, yellow solid, m.p.: 215−216 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.2 Hz, 2H), 7.76−7.69 (m, 2H), 7.49−7.41 (m, 3H), 7.31−7.20 (m, 4H), 7.12 (d, *J* = 8.2 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.85 (s, 1H), 4.95−4.79 (m, 1H), 3.56−3.45 (m, 1H), 3.43−3.31 (m, 1H), 2.41 (s, 3H), 1.58−1.44 (m, 8H), 1.36−1.22 (m, 2H), 0.85 (t, *J* = 7.4 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 172.1, 165.2, 159.7, 141.8, 141.3, 140.3, 135.1, 133.3, 130.7, 128.9, 128.9, 128.8, 126.9, 126.5, 123.7, 122.8, 111.3, 108.7, 65.6, 54.1, 47.0, 33.0, 21.6, 20.5, 19.2, 19.1, 14.0. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{31}H_{34}N_3O_2S_2$: 544.2092; found: 544.2089.

*N-(1-Isopropyl-5′-phenyl-3′-(phenylimino)-3′H-spiro[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**3z3**).* Following the general procedure, compound **3z3** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 130 mg, 77% yield, orange solid, m.p.: 222−223 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.1 Hz, 2H), 7.61 (d, *J* = 6.2 Hz, 2H), 7.46−7.26 (m, 7H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.18−7.03 (m, 3H), 6.92 (d, *J* = 7.6 Hz, 2H), 6.66 (s, 1H), 4.97−4.72 (m, 1H), 2.39 (s, 3H), 1.61−1.38 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 173.9, 164.2, 162.4, 151.8, 142.1, 141.0, 140.3, 134.4, 132.8, 131.1, 129.2, 129.1, 128.9, 128.9, 126.9, 126.5, 124.0, 123.9, 122.8, 120.8, 111.5, 110.7, 65.6, 47.2, 21.6, 19.2, 19.2. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{33}H_{30}N_3O_2S_2$: 564.1779; found: 564.1776.

*Typical Procedure for the Preparation of 5: The Synthesis of 3′-(Benzylimino)-1-methyl-5′-phenyl-3′H-spiro[indoline-3,2′-thiophen]-2-one (**5a**).* A mixture of **1a** (90 mg, 0.3 mmol), **4a** (78 mg, 0.45 mmol), and CuCN (2.7 mg, 0.03 mmol) in 3 mL of toluene was vigorously stirred at 110 °C for 5 h under a nitrogen atmosphere. After cooling to ambient temperature, all of the volatiles were evaporated under reduced pressure. The resultant residue was purified by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/ethyl acetate = 8:1, v/v) to afford product **5a** (95 mg, 80%).

*3′-(Benzylimino)-1-methyl-5′-phenyl-3′H-spiro[indoline-3,2′-thiophen]-2-one (**5a**).* Following the general procedure, compound **5a** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 95 mg, 80% yield, yellow solid, m.p.: 171−172 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73−7.65 (m, 2H), 7.50−7.43 (m, 3H), 7.36 (m, 1H), 7.32−7.25 (m, 3H), 7.20 (t, *J* = 7.3 Hz, 1H), 7.13 (m, 3H), 6.91 (d, *J* = 7.8 Hz,

https://doi.org/10.1021/acs.joc.2c00137
J. Org. Chem. 2022, 87, 4424−4437

1H), 6.80 (s, 1H), 4.77 (q, J = 15.3 Hz, 2H), 3.30 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 174.6, 174.2, 162.3, 144.4, 139.7, 132.9, 131.2, 130.6, 129.6, 129.0, 128.4, 127.0, 127.0, 126.6, 124.5, 123.4, 109.0, 108.2, 65.0, 57.6, 27.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{25}H_{21}N_2OS$: 397.1375; found: 397.1380.

*3′-(Benzylimino)-1-isopropyl-5′-phenyl-3′H-spiro[indoline-3,2′-thiophen]-2-one (**5b**).* Following the general procedure, compound **5b** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 100 mg, 78% yield, yellow solid, m.p.: 157−158 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.71−7.65 (m, 2H), 7.48−7.41 (m, 3H), 7.33−7.22 (m, 4H), 7.17 (t, J = 6.8 Hz, 3H), 7.11−7.01 (m, 2H), 6.76 (s, 1H), 4.80−4.65 (m, 2H), 4.65−4.56 (m, 1H), 1.58−1.48 (m, 6H).$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 174.3, 173.9, 143.4, 140.0, 133.0, 131.2, 129.3, 128.9, 128.3, 127.1, 127.0, 126.5, 124.8, 122.8, 110.3, 108.0, 65.1, 57.4, 45.0, 19.6, 19.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{27}H_{25}N_2OS$: 425.1688; found: 425.1685.

*1-Benzyl-3′-(benzylimino)-5′-phenyl-3′H-spiro[indoline-3,2′-thiophen]-2-one (**5c**).* Following the general procedure, compound **5c** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 122 mg, 86% yield, yellow solid, m.p.: 164−165 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.80−7.70 (m, 2H), 7.54−7.46 (m, 3H), 7.45−7.39 (m, 2H), 7.36−7.29 (m, 3H), 7.28−7.18 (m, 7H), 7.14−7.05 (m, 1H), 6.88 (s, 1H), 6.73 (d, J = 7.8 Hz, 1H), 5.25 (d, J = 16.0 Hz, 1H), 4.89−4.68 (m, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 174.4, 174.2, 143.4, 139.8, 135.1, 132.9, 131.3, 129.5, 129.0, 128.8, 128.4, 127.5, 127.3, 127.2, 127.0, 126.6, 124.5, 123.4, 109.9, 108.0, 65.1, 57.7, 44.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{31}H_{25}N_2OS$: 473.1688; found: 473.1689.

*1-Benzyl-3′-(benzylimino)-4-chloro-5′-phenyl-3′H-spiro[indoline-3,2′-thiophen]-2-one (**5d**).* Following the general procedure, compound **5d** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 103 mg, 68% yield, yellow solid, m.p.: 157−158 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 6.3 Hz, 2H), 7.55−7.45 (m, 3H), 7.41−7.20 (m, 10H), 7.16 (t, J = 7.9 Hz, 1H), 7.04 (d, J = 8.2 Hz, 1H), 6.97 (s, 1H), 6.63 (d, J = 7.7 Hz, 1H), 5.14 (d, J = 15.9 Hz, 1H), 4.96−4.69 (m, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.9, 172.7, 162.1, 145.3, 139.7, 134.8, 133.0, 131.7, 131.2, 130.7, 129.1, 129.0, 128.9, 128.4, 127.7, 127.5, 127.1, 127.0, 126.7, 124.1, 109.6, 108.2, 64.8, 57.9, 44.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{31}H_{25}N_2OS$: 507.1298; found: 507.1300.

*1-Benzyl-3′-(benzylimino)-5-methoxy-5′-phenyl-3′H-spiro[indoline-3,2′-thiophen]-2-one (**5e**).* Following the general procedure, compound **5e** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 119 mg, 79% yield, yellow solid, m.p.: 170−171 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.77−7.68 (m, 2H), 7.53−7.43 (m, 3H), 7.38 (d, J = 6.4 Hz, 2H), 7.33−7.27 (m, 2H), 7.26−7.15 (m, 6H), 6.90 (d, J = 2.5 Hz, 1H), 6.85 (s, 1H), 6.74 (m, 1H), 6.59 (d, J = 8.6 Hz, 1H), 5.19 (d, J = 16.0 Hz, 1H), 4.85−4.67 (m, 3H), 3.73 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 174.2, 156.5, 139.8, 136.7, 135.2, 132.9, 131.7, 131.3, 129.0, 128.8, 128.4, 127.5, 127.4, 127.2, 127.0, 126.6, 114.5, 111.2, 110.4, 108.0, 65.4, 57.7, 55.9, 44.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{32}H_{27}N_2O_2S$: 503.1793; found: 503.1800.

*1-Benzyl-3′-(benzylimino)-5-nitro-5′-phenyl-3′H-spiro[indoline-3,2′-thiophen]-2-one (**5f**).* Following the general procedure, compound **5f** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 126 mg, 81% yield, orange solid, m.p.: 166−167 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.19−8.10 (m, 2H), 7.71 (dd, J = 7.8, 1.6 Hz, 2H), 7.57−7.45 (m, 3H), 7.33−7.26 (m, 3H), 7.26−7.20 (m, 3H), 7.19−7.12 (m, 4H), 6.84 (s, 1H), 6.74 (d, J = 8.5 Hz, 1H), 5.30 (d, J = 16.0 Hz, 1H), 4.72 (m, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 174.6, 173.3, 162.6, 149.2, 144.0, 139.4, 134.0, 132.6, 131.9, 131.7, 129.19, 129.1, 128.5, 128.0, 127.5, 127.2, 127.1, 126.9, 126.5, 120.6, 109.6, 107.9, 64.23, 58.0, 44.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{31}H_{24}N_3O_3S$: 518.1538; found: 503.1542.

*1-Benzyl-3′-(benzylimino)-5-iodo-5′-phenyl-3′H-spiro[indoline-3,2′-thiophen]-2-one (**5g**).* Following the general procedure, compound **5g** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 145 mg, 81% yield, yellow solid, m.p.: 185−186 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.74−7.64 (m, 2H), 7.55 (d, J = 1.6 Hz, 1H), 7.51−7.43 (m, 4H), 7.35−7.26 (m, 4H), 7.24−7.12 (m, 6H), 6.80 (s, 1H), 6.43 (d, J = 8.3 Hz, 1H), 5.20 (d, J = 16.0 Hz, 1H), 4.78 (d, J = 15.7 Hz, 1H), 4.74−4.64 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.8, 173.8, 162.4, 143.2, 139.8, 138.2, 134.7, 133.2, 133.1, 132.8, 131.4, 129.1, 128.9, 128.5, 127.7, 127.4, 127.2, 127.0, 126.7, 111.9, 107.9, 85.7, 64.6, 57.9, 44.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{32}H_{27}N_2O_2S$: 599.0654; found: 99.0652.

*1-Benzyl-3′-(benzylimino)-6-fluoro-5′-phenyl-3′H-spiro[indoline-3,2′-thiophen]-2-one (**5h**).* Following the general procedure, compound **5h** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 118 mg, 80% yield, yellow solid, m.p.: 181−182 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 7.4 Hz, 2H), 7.55−7.46 (m, 3H), 7.37 (d, J = 7.3 Hz, 2H), 7.34−7.29 (m, 2H), 7.28−7.17 (m, 7H), 6.85 (s, 1H), 6.76 (dd, J = 12.3, 5.3 Hz, 1H), 6.46 (d, J = 8.7 Hz, 1H), 5.21 (d, J = 16.0 Hz, 1H), 4.87−4.65 (m, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 174.7, 174.0, 164.8, 162.3, 145.0 (d, $J_{C\text{-}F}$ = 11.7 Hz), 139.7, 134.6, 132.8, 131.4, 129.0, 128.9, 128.4, 127.7, 127.4, 127.2, 127.0, 126.7, 125.7 (d, $J_{C\text{-}F}$ = 10.0 Hz), 109.7 (d, $J_{C\text{-}F}$ = 22.8 Hz), 107.9, 98.7 (d, $J_{C\text{-}F}$ = 27.9 Hz), 64.6, 57.7, 44.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{31}H_{24}FN_2OS$: 491.1593; found: 491.1590.

*1-Benzyl-3′-(benzylimino)-7-methyl-5′-phenyl-3′H-spiro[indoline-3,2′-thiophen]-2-one (**5i**).* Following the general procedure, compound **5i** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 118 mg, 81% yield, yellow solid, m.p.: 179−180 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.77−7.67 (m, 2H), 7.51−7.42 (m, 3H), 7.33 (d, J = 6.8 Hz, 2H), 7.30−7.26 (m, 2H), 7.25−7.21 (m, 3H), 7.21−7.10 (m, 4H), 6.97 (t, J = 4.6 Hz, 2H), 6.83 (s, 1H), 5.47 (d, J = 16.9 Hz, 1H), 5.03 (d, J = 16.9 Hz, 1H), 4.77 (dd, J = 38.7, 15.6 Hz, 2H), 2.25 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 175.4, 174.6, 162.5, 141.5, 139.9, 137.1, 133.5, 133.1, 131.5, 131.2, 129.0, 128.9, 128.4, 127.5, 127.1, 127.0, 126.6, 126.0, 123.5, 122.7, 120.6, 107.9, 64.8, 57.9, 45.7, 18.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{31}H_{24}FN_2OS$: 487.1844; found: 487.1855.

*1-Benzyl-3′-(benzylimino)-5′-(o-tolyl)-3′H-spiro[indoline-3,2′-thiophen]-2-one (**5j**).* Following the general procedure, compound **5j** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 124 mg, 85% yield, yellow solid, m.p.: 169−170 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.61−7.55 (m, 1H), 7.42−7.26 (m, 9H), 7.28−7.16 (m, 7H), 7.13−7.07 (m, 1H), 6.72 (d, J = 7.8 Hz, 1H), 6.46 (s, 1H), 5.23 (d, J = 16.0 Hz, 1H), 4.83−4.72 (m, 2H), 4.67 (d, J = 15.7 Hz, 1H), 2.58 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 174.4, 174.2, 163.6, 143.4, 139.8, 136.0, 135.2, 133.4, 131.1, 130.4, 130.0, 129.4, 128.8, 128.7, 128.3, 127.5, 127.3, 127.2, 126.6, 126.2, 124.4, 123.3, 112.4, 109.9, 65.8, 57.6, 44.2, 20.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{32}H_{27}N_2OS$: 487.1844; found: 487.1840.

*1-Benzyl-3′-(benzylimino)-5′-(3-methoxyphenyl)-3′H-spiro[indoline-3,2′-thiophen]-2-one (**5k**).* Following the general procedure, compound **5k** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 119 mg, 79% yield, yellow solid, m.p.: 173−174 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.43−7.38 (m, 3H), 7.36−7.29 (m, 4H), 7.27−7.17 (m, 8H), 7.11−7.03 (m, 2H), 6.84 (s, 1H), 6.72 (d, J = 7.8 Hz, 1H), 5.24 (d, J = 16.0 Hz, 1H), 4.87−4.77 (m, 2H), 4.73 (d, J = 15.7 Hz, 1H), 3.89 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 174.3, 174.2, 159.9, 143.4, 139.8, 135.1, 134.2, 130.0, 129.5, 128.8, 128.4, 127.5, 127.4, 127.2, 126.6, 124.5, 123.4, 119.5, 117.0, 112.3, 110.0, 108.3, 65.2, 57.6, 55.5, 44.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{32}H_{27}N_2O_2S$: 503.1793; found: 503.1791.

*1-Benzyl-3′-(benzylimino)-5′-(4-methoxyphenyl)-3′H-spiro[indoline-3,2′-thiophen]-2-one (**5l**).* Following the general procedure, compound **5l** was obtained by column chromatography on silica

https://doi.org/10.1021/acs.joc.2c00137
J. Org. Chem. 2022, 87, 4424−4437

gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 113 mg, 75% yield, yellow solid, m.p.: 193−194 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.8 Hz, 2H), 7.24 (d, *J* = 6.7 Hz, 2H), 7.19−6.99 (m, 10H), 6.91 (t, *J* = 7.5 Hz, 1H), 6.82 (d, *J* = 8.8 Hz, 2H), 6.61 (s, 1H), 6.54 (d, *J* = 7.8 Hz, 1H), 5.07 (d, *J* = 16.0 Hz, 1H), 4.64 (dd, *J* = 15.8, 8.3 Hz, 2H), 4.54 (d, *J* = 15.7 Hz, 1H), 3.70 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 174.6, 174.3, 162.0, 161.9, 143.4, 140.0, 135.1, 130.8, 129.3, 128.7, 128.6, 128.3, 127.4, 127.3, 127.1, 126.5, 125.5, 124.4, 123.3, 114.3, 109.8, 106.3, 65.0, 57.6, 55.5, 44.1. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{31}H_{24}BrN_2OS$: 503.1793; found: 503.1811.

*1-Benzyl-3′-(benzylimino)-5′-(4-bromophenyl)-3′H-spiro-[indoline-3,2′-thiophen]-2-one (**5m**).* Following the general procedure, compound **5m** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 136 mg, 82% yield, yellow solid, m.p.: 211−212 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 1.4 Hz, 1H), 7.36 (m, 2H), 7.27 (m, 4H), 7.23−7.13 (m, 7H), 7.06 (td, *J* = 7.6, 0.8 Hz, 1H), 6.85 (d, *J* = 3.3 Hz, 1H), 6.76 (s, 1H), 6.69 (d, *J* = 7.8 Hz, 1H), 6.55 (dd, *J* = 3.5, 1.8 Hz, 1H), 5.20 (d, *J* = 16.0 Hz, 1H), 4.77 (d, *J* = 15.7 Hz, 2H), 4.67 (d, *J* = 15.7 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 174.3, 173.8, 148.0, 145.3, 143.5, 139.8, 135.1, 129.6, 128.8, 128.3, 127.5, 127.4, 127.2, 126.6, 124.6, 123.4, 113.6, 112.8, 109.9, 106.2, 64.7, 57.7, 44.2. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{31}H_{24}BrN_2OS$: 551.0793; found: 551.0794.

*1-Benzyl-3′-(benzylimino)-5′-(4-(trifluoromethyl)phenyl)-3′H-spiro[indoline-3,2′-thiophen]-2-one (**5n**).* Following the general procedure, compound **5n** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 138 mg, 85% yield, yellow solid, m.p.: 174−175 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.2 Hz, 2H), 7.73 (d, *J* = 8.3 Hz, 2H), 7.39 (d, *J* = 6.6 Hz, 2H), 7.33−7.27 (m, 3H), 7.26−7.16 (m, 7H), 7.08 (td, *J* = 7.6, 0.8 Hz, 1H), 6.93 (s, 1H), 6.72 (d, *J* = 7.8 Hz, 1H), 5.24 (d, *J* = 16.0 Hz, 1H), 4.87−4.69 (m, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 174.2, 173.7, 160.5, 143.4, 139.6, 136.3, 135.0, 132.6 (q, $J_{C\text{-}F}$ = 32.8 Hz) 130.3, 129.7, 128.8, 128.4, 127.5, 127.3, 127.3, 127.1, 126.7, 126.0, 125.9, 124.5, 123.4, 110.0, 109.6, 65.3, 57.9, 44.2. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{32}H_{24}F_3N_2OS$: 541.1561; found: 541.1566.

*1-Benzyl-3′-(benzylimino)-5′-(furan-2-yl)-3′H-spiro[indoline-3,2′-thiophen]-2-one (**5o**).* Following the general procedure, compound **5o** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 106 mg, 76% yield, yellow solid, m.p.: 165−166 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64−7.53 (m, 4H), 7.37 (d, *J* = 6.6 Hz, 2H), 7.28 (t, *J* = 5.2 Hz, 2H), 7.24−7.15 (m, 7H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.82 (s, 1H), 6.70 (d, *J* = 7.8 Hz, 1H), 5.21 (d, *J* = 16.0 Hz, 1H), 4.84−4.74 (m, 2H), 4.70 (d, *J* = 15.7 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 174.2, 174.1, 143.5, 139.6, 135.1, 132.2, 131.8, 129.6, 128.8, 128.4, 127.6, 127.3, 127.2, 126.7, 124.5, 123.4, 110.0, 108.4, 65.3, 57.7, 44.3. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{29}H_{23}N_2O_2S$: 463.1480; found: 463.1474.

*Gram-Scale Synthesis of **3a**.* A mixture of **1a** (1.20 g, 4.0 mmol), **2a** (2.12 g, 6.0 mmol), and $Cu(MeCN)_4BF_4$ (126 mg, 0.4 mmol) in 20 mL of toluene was vigorously stirred at 110 °C for 2 h under a nitrogen atmosphere. After cooling to ambient temperature, all of the volatiles were evaporated under reduced pressure. The resultant residue was purified by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/ethyl acetate = 10:1, v/v) to afford product **3a** (1.85 g, 80%).

*Gram-Scale Synthesis of **5c**.* A mixture of **1a** (1.20 g, 4.0 mmol), **4c** (1.50 g, 6.0 mmol), and CuCN (36 mg, 0.4 mmol) in 20 mL of toluene was vigorously stirred at 110 °C for 7 h under a nitrogen atmosphere. After cooling to ambient temperature, all of the volatiles were evaporated under reduced pressure. The resultant residue was purified by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/ethyl acetate = 8:1, v/v) to afford product **5c** (1.47 g, 78%).

*Typical Procedure for the Preparation of 6: The Synthesis of 1-Benzyl-5′-phenyl-3′H-spiro[indoline-3,2′-thiophene]-2,3′-dione (**6b**).* A mixture of 2-imine-dihydrothiophenes **5c** (95 mg, 0.2 mmol), H_2SO_4(10% aq, 0.2 mL), and EtOH (2 mL) was stirred at reflux for 12 h, cooled to ambient temperature, and then evaporated all of the volatiles under reduced pressure. The resultant residue was purified by silica gel column chromatography (eluent: petroleum ether (60−90 °C)/AcOEt = 10:1, v/v), affording **6b** as a yellow solid (70 mg, 91%).

*1-Isopropyl-5′-phenyl-3′H-spiro[indoline-3,2′-thiophene]-2,3′-dione (**6a**).* Following the general procedure, compound **6a** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 56 mg, 84% yield, red solid, m.p.: 80−81 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.3 Hz, 2H), 7.57 (t, *J* = 7.3 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 2H), 7.38−7.30 (m, 1H), 7.20 (d, *J* = 7.3 Hz, 1H), 7.12−7.02 (m, 2H), 6.50 (s, 1H), 4.67−4.54 (m, 1H), 1.48−1.58 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 197.7, 178.5, 170.5, 144.0, 132.9, 132.3, 129.9, 129.2, 127.1, 126.8, 124.5, 123.0, 114.83, 110.65, 67.0, 45.3, 19.6, 19.4. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{20}H_{18}NO_2S$: 336.1058; found: 336.1073.

*1-Benzyl-5′-phenyl-3′H-spiro[indoline-3,2′-thiophene]-2,3′-dione (**6b**).* Following the general procedure, compound **6b** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 70 mg, 91% yield, yellow solid, m.p.: 83−84 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77−7.67 (m, 2H), 7.55−7.48 (m, 1H), 7.48−7.41 (m, 2H), 7.33−7.24 (m, 4H), 7.22−7.12 (m, 3H), 6.97 (td, *J* = 7.6, 0.7 Hz, 1H), 6.68 (d, *J* = 7.8 Hz, 1H), 6.47 (s, 1H), 5.03 (d, *J* = 15.9 Hz, 1H), 4.78 (d, *J* = 15.9 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 197.7, 178.6, 171.2, 144.2, 135.0, 133.0, 132.2, 130.2, 129.3, 129.0, 127.9, 127.3, 127.2, 126.5, 124.3, 123.6, 114.9, 110.2, 66.9, 44.7. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{31}H_{25}NO_2S$: 384.1058; found: 384.1050.

*1-Benzyl-7-methyl-5′-phenyl-3′H-spiro[indoline-3,2′-thiophene]-2,3′-dione (**6c**).* Following the general procedure, compound **6c** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 70 mg, 88% yield, red solid, m.p.: 95−96 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.0 Hz, 1H), 7.41 (dt, *J* = 27.6, 7.7 Hz, 1H), 7.30−7.17 (m, 1H), 7.14 (t, *J* = 6.3 Hz, 1H), 6.98 (d, *J* = 6.6 Hz, 1H), 6.91−6.82 (m, 1H), 6.42 (d, *J* = 0.9 Hz, 1H), 5.26 (d, *J* = 16.9 Hz, 1H), 4.97 (d, *J* = 16.9 Hz, 1H), 2.15 (s, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 197.8, 178.6, 172.0, 142.1, 136.8, 134.0, 132.9, 132.1, 129.2, 129.0, 127.3, 127.0, 126.9, 125.7, 123.6, 122.2, 120.9, 114.6, 66.5, 45.8, 18.7. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{25}H_{20}NO_2S$: 398.1215; found: 398.1201.

*1-Benzyl-5′-(4-methoxyphenyl)-3′H-spiro[indoline-3,2′-thiophene]-2,3′-dione (**6d**).* Following the general procedure, compound **6d** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v). 73 mg, 89% yield, yellow solid, m.p.: 87−88 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 6.6 Hz, 2H), 7.34−7.22 (m, 4H), 7.22−7.10 (m, 3H), 7.01−6.86 (m, 3H), 6.66 (d, *J* = 6.2 Hz, 1H), 6.38 (s, 1H), 5.02 (d, *J* = 15.9 Hz, 1H), 4.77 (d, *J* = 15.8 Hz, 1H), 3.81 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 197.4, 178.0, 171.5, 163.6, 144.1, 135.0, 130.0, 129.1, 129.0, 127.8, 127.2, 126.7, 124.8, 124.3, 123.6, 114.6, 112.9, 110.2, 66.7, 55.7, 44.6. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{25}H_{20}NO_3S$: 414.1164; found: 414.1167.

Click Reaction of Compound 3z1. A mixture of 2-imine-dihydrothiophenes **3z1** (158 mg, 0.3 mmol), benzyl azide (60 mg, 0.45 mmol), $CuSO_4{\cdot}5H_2O$ (7.5 mg, 0.03 mmol), and sodium ascorbate (30 mg, 0.15 mmol) in THF (2.5 mL) and H_2O (0.5 mL) was stirred at 25 °C for 24 h and then evaporated all of the volatiles under reduced pressure. The resultant residue was purified by silica gel column chromatography (eluent: petroleum ether (60−90 °C)/AcOEt = 10:1, v/v), affording **7** as a yellow oil (170 mg, 86%).

*N-(3′-(((1-Benzyl-1H-1,2,3-triazol-4-yl)methyl)imino)-1-isopropyl-5′-phenyl-3′H-spiro[indoline-3,2′-thiophen]-2-ylidene)-4-methylbenzenesulfonamide (**7**).* Following the general procedure, compound **7** was obtained by column chromatography on silica gel (eluent: petroleum ether (60−90 °C)/EtOAc = 10:1, v/v). 170 mg, 86% yield, yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72−7.55 (m, 4H), 7.44−7.32 (m, 3H), 7.24−7.15 (m, 4H), 7.15−7.09 (m, 2H),

https://doi.org/10.1021/acs.joc.2c00137
J. Org. Chem. 2022, 87, 4424−4437

7.09−7.02 (m, 4H), 7.00 (d, J = 7.7 Hz, 1H), 6.90 (t, J = 7.4 Hz, 1H), 6.77 (s, 1H), 5.22 (s, 2H), 4.88−4.57 (m, 3H), 2.29 (s, 3H), 1.46−1.28 (m, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 175.2, 164.6, 162.0, 147.7, 142.1, 140.8, 140.2, 135.0, 134.5, 132.9, 131.2, 129.1, 129.0, 129.0, 128.5, 128.1, 127.0, 126.5, 123.9, 122.9, 122.2, 111.5, 108.8, 65.7, 54.0, 50.0, 47.2, 21.6, 19.2, 19.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{37}H_{35}N_6O_2S_2$: 659.2263; found: 659.2262.

TEMPO or BHT-Trapping Radical Experiments. Under a nitrogen atmosphere, a mixture of enaminothione **1a** (90 mg, 0.3 mmol), diazo compound **2a** (159 mg, 0.45 mmol), TEMPO (71 mg, 0.45 mmol), and $Cu(MeCN)_4BF_4$ (9.4 mg, 0.03 mmol) in 2 mL of toluene was stirred at 110 °C for 2 h. The reaction mixture was cooled to ambient temperature, filtered through a short pad of Celite, rinsed with 20 mL of ethyl acetate, and evaporated all of the volatiles under reduced pressure. The resultant residue was purified by silica gel column chromatography (eluent: petroleum ether (60−90 °C)/AcOEt = 30:1, v/v), affording **3a** as an orange solid (127 mg, 73%). A mixture of enaminothione **1a** (90 mg, 0.3 mmol), diazo compound **2a** (159 mg, 0.45 mmol), BHT (99 mg, 0.45 mmol), and $Cu(MeCN)_4BF_4$ (9.4 mg, 0.03 mmol) in 2 mL of toluene was stirred at 110 °C for 2 h. The reaction mixture was cooled to ambient temperature, filtered through a short pad of Celite, rinsed with 20 mL of ethyl acetate, and evaporated all of the volatiles under reduced pressure. The resultant residue was purified by silica gel column chromatography (eluent: petroleum ether (60−90 °C)/AcOEt = 30:1, v/v), affording **3a** as an orange solid (135 mg, 78%).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.2c00137.

Experimental materials and procedures; analytical data and NMR spectra of compounds; X-ray crystallographic analysis for **5a** (PDF)

Accession Codes

CCDC 2022791 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.

■ AUTHOR INFORMATION

Corresponding Authors

Zhengkun Yu − *Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian 116023, P. R. China; Innovation Academy for Green Manufacture, Chinese Academy of Sciences, Beijing 100190, P. R. China; State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, P. R. China;* orcid.org/0000-0002-9908-0017; Email: zkyu@dicp.ac.cn

Yong-Gui Zhou − *Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian 116023, P. R. China;* orcid.org/0000-0002-3321-5521; Email: ygzhou@dicp.ac.cn

Authors

Zilong Huang − *Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian 116023, P. R. China; University of Chinese Academy of Sciences, Beijing 100049, P. R. China;* orcid.org/0000-0001-5350-8308

Yuan He − *Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian 116023, P. R. China; University of Chinese Academy of Sciences, Beijing 100049, P. R. China;* orcid.org/0000-0001-6600-8433

Liandi Wang − *Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian 116023, P. R. China;* orcid.org/0000-0003-4996-3687

Jiying Li − *East China University of Science and Technology, Shanghai 200237, P. R. China*

Bao-Hua Xu − *Innovation Academy for Green Manufacture, Chinese Academy of Sciences, Beijing 100190, P. R. China;* orcid.org/0000-0002-7222-4383

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.joc.2c00137

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors are grateful to the National Natural Science Foundation of China (22171261, 21871253).

■ REFERENCES

(1) (a) Xia, Y.; Wang, J. B. Transition-Metal-Catalyzed Cross-Coupling with Ketones or Aldehydes *via N*-Tosylhydrazones. *J. Am. Chem. Soc.* **2020**, *142*, 10592−10605. (b) Zhu, D.; Chen, L. F.; Fan, H. L.; Yao, Q. L.; Zhu, S. F. Recent Progress on Donor and Donor−Donor Carbenes. *Chem. Soc. Rev.* **2020**, *49*, 908−950.

(2) (a) Cui, X.-Y.; Zhao, Y.-L.; Chen, Y.-M.; Dong, S.-Z.; Zhou, F.; Wu, H.-H.; Zhou, J. Au-Catalyzed Formal Allylation of Diazo(thio)-oxindoles: Application to Tandem Asymmetric Synthesis of Quaternary Stereocenters. *Org. Lett.* **2021**, *23*, 4864−4869. (b) Yang, Z.; Möller, M.; Koenigs, R. M. Synthesis of *gem*-Difluoro Olefins through C−H Functionalization and β-Fluoride Elimination Reactions. *Angew. Chem., Int. Ed.* **2020**, *59*, 5572−5576. (c) Xiang, Y. Y.; Wang, C.; Ding, Q. P.; Peng, Y. Y. Diazo Compounds: Versatile Synthons for the Synthesis of Nitrogen Heterocycles *via* Transition Metal-Catalyzed Cascade C−H Activation/Carbene Insertion/Annulation Reactions. *Adv. Synth. Catal.* **2019**, *361*, 919−944. (d) Wang, B.; Howard, I. G.; Pope, J. W.; Conte, E. D.; Deng, Y. M. Bis(imino)pyridine Iron Complexes for Catalytic Carbene Transfer Reactions. *Chem. Sci.* **2019**, *10*, 7958−7963. (e) Jana, S.; Koenigs, R. M. Rhodium-Catalyzed Carbene Transfer Reactions for Sigmatropic Rearrangement Reactions of Selenium Ylides. *Org. Lett.* **2019**, *21*, 3653−3657.

(3) (a) Jana, S.; Empel, C.; Pei, C.; Aseeva, P.; Nguyen, T. V.; Koenigs, R. M. C−H Functionalization Reactions of Unprotected *N*-Heterocycles by Gold-Catalyzed Carbene Transfer. *ACS Catal.* **2020**, *10*, 9925−9931. (b) Yang, Y. Q.; Qiu, X. D.; Zhao, Y.; Mu, Y. C.; Shi, Z. Z. Palladium-Catalyzed C−H Arylation of Indoles at the C7 Position. *J. Am. Chem. Soc.* **2016**, *138*, 495−498.

(4) (a) Xia, Y.; Qiu, D.; Wang, J. B. Transition-Metal-Catalyzed Cross-Couplings Through Carbene Migratory Insertion. *Chem. Rev.* **2017**, *117*, 13810−13889. (b) Ford, A.; Miel, H.; Ring, A.; Slattery, C. N.; Maguire, A. R.; et al. Modern Organic Synthesis with α-Diazocarbonyl Compounds. *Chem. Rev.* **2015**, *115*, 9981−10080.

(5) (a) Massaro, N. P.; Stevens, J. C.; Chatterji, A.; Sharma, I. Stereoselective Synthesis of Diverse Lactones through a Cascade Reaction of Rhodium Carbenoids with Ketoacids. *Org. Lett.* **2018**, *20*, 7585−7589. (b) Choi, S. B.; Ha, S. J.; Park, C.-M. α-Diazo Oxime Ethers for *N*-Heterocycle Synthesis. *Chem. Commun.* **2017**, *53*, 6054−6064. (c) Hu, F.; Zhou, Q.; Cao, F.; Chu, W.-D.; He, L.; Liu, Q.-Z. Enantioselective Formal [4+1] Cycloaddition of Diazoarylacetates and the Danishefsky's Diene: Stereoselective Synthesis of (−)-1,13-Herbertenediol. *J. Org. Chem.* **2018**, *83*, 12806−12814.

(6) Cao, Z.-Y.; Zhou, F.; Zhou, J. Development of Synthetic Methodologies *via* Catalytic Enantioselective Synthesis of 3,3-Disubstituted Oxindoles. *Acc. Chem. Res.* **2018**, *51*, 1443−1454.

(7) Santos, M. M. Recent Advances in the Synthesis of Biologically Active Spirooxindoles. *Tetrahedron* **2014**, *70*, 9735−9757.
(8) Ding, K.; Lu, Y. P.; Nikolovska-Coleska, Z.; Wang, G. P.; Qiu, S.; Shangary, S. J.; Gao, W.; Qin, D. G.; Stukey, J.; Krajewski, K.; Roller, P. P.; Wang, S. M. Structure-Based Design of Spiro-oxindoles as Potent, Specific Small-Molecule Inhibitors of the MDM2-p53 Interaction. *J. Med. Chem.* **2006**, *49*, 3432−3435.
(9) Xiao, G. L.; Chen, T. T.; Ma, C. Q.; Xing, D.; Hu, W. H. Rh(II)/Chiral Phosphoric Acid-Cocatalyzed Enantioselective Synthesis of Spirooxindole-Fused Thiaindans. *Org. Lett.* **2018**, *20*, 4531−4535.
(10) Liu, Y.; Huang, Q.-Z.; Li, Q.-Z.; Leng, H.-J.; Dai, Q.-S.; Zeng, R.; Liu, Y.-Q.; Zhang, X.; Han, B.; Li, J.-L. Highly Chemo- and Diastereoselective Construction of Quaternary Stereocenters Through Palladium-Catalyzed [3+2] Cyclization of 5-Alkenyl Thiazolones. *Org. Lett.* **2019**, *21*, 7478−7483.
(11) Wang, S. Z.; Jiang, Y.; Wu, S. C.; Dong, G. Q.; Miao, Z. Y.; Zhang, W. N.; Sheng, C. Q. Meeting Organocatalysis with Drug Discovery: Asymmetric Synthesis of 3,3′-Spirooxindoles Fused with Tetrahydrothiopyrans as Novel p53-MDM2 Inhibitors. *Org. Lett.* **2016**, *18*, 1028−1031.
(12) Zhou, Y.; Huang, Y. L.; Tang, G. H.; Li, X. F. Synthesis of Dispiro[1-benzothiophene-2,3′-pyrrolidine-2′,3”-indoline]-2”,3-diones in Cycloaddition Reaction. *Chem. Heterocycl. Compd.* **2019**, *55*, 1044−1049.
(13) (a) Song, L. L.; Ni, D.; Jia, S. K.; Pi, R.; Dong, S. Z.; Yang, F.; Tang, J.; Liu, S. Y. C(sp^2)−H Bond Multiple Functionalization in Air for Construction of Tetrahydrocarbazoles with Continuous Quaternary Carbons and Polycyclic Diversification. *Org. Lett.* **2020**, *22*, 1846−1851. (b) Reddy, A. C. S.; Reddy, P. M.; Anbarasan, P. Diastereoselective Palladium Catalyzed Carbenylative Amination of *ortho*-Vinylanilines with 3-Diazoindolin-2-ones. *Adv. Synth. Catal.* **2020**, *362*, 801−806. (c) Gopi Krishna Reddy, A.; Niharika, P.; Zhou, S.; Jia, S.-K.; Shi, T. D.; Xu, X. F.; Qian, Y.; Hu, W. H. Brønsted Acid Catalyzed Enantioselective Assembly of Spirochroman-3,3-oxindoles. *Org. Lett.* **2020**, *22*, 2925−2930. (d) Ma, B.; Wu, P.; Wang, X.; Wang, Z. Y.; Lin, H.-X.; Dai, H.-X. Efficient Synthesis of Spirooxindole Pyrrolones by a Rhodium(III)-Catalyzed C−H Activation/Carbene Insertion/Lossen Rearrangement Sequence. *Angew. Chem., Int. Ed.* **2019**, *58*, 13335−13339.
(14) (a) Zhao, S.; Chen, X.-X.; Gao, N.; Qian, M. C.; Chen, X. Visible-Light-Mediated Cyclopropanation Reactions of 3-Diazooxindoles with Arenes. *J. Org. Chem.* **2021**, *86*, 7131−7140. (b) Rodriguez, K. X.; Kaltwasser, N.; Toni, T. A.; Ashfeld, B. L. Rearrangement of an Intermediate Cyclopropyl Ketene in a Rh(II)-Catalyzed Formal [4+1]-Cycloaddition Employing Vinyl Ketenes as 1,4-Dipoles and Donor-Acceptor Metallocarbenes. *Org. Lett.* **2017**, *19*, 2482−2485. (c) Meloche, J. L.; Ashfeld, B. L. A Rhodium(II)-Catalyzed Formal [4+1]-Cycloaddition toward Spirooxindole Pyrrolone Construction Employing Vinyl Isocyanates as 1,4-Dipoles. *Angew. Chem., Int. Ed.* **2017**, *56*, 6604−6608. (d) Cao, F.; Hu, F.; Xie, Q.-M.; Luo, G.-Y.; Chu, W.-D.; He, L.; Liu, Q.-Z. Rhodium-Catalyzed Enantioselective Formal [4+1] Cycloaddition of Diazooxindoles and the Danishefsky Diene. *Asian J. Org. Chem.* **2018**, *7*, 363−366.
(15) (a) Lang, B.; Zhu, H. T. Z.; Wang, C.; Lu, P.; Wang, Y. G. Rhodium-Catalyzed Cycloadditions Between 3-Diazoindolin-2-imines and 1,3-Dienes. *Org. Lett.* **2017**, *19*, 1630−1633. (b) Ding, H. L.; Wang, Z. B.; Bai, S. L.; Lu, P.; Wang, Y. G. Rh-Catalyzed Conversion of 3-Diazoindolin-2-imines to 5*H*-Pyrazino[2,3-*b*]indoles with Photoluminescent Properties. *Org. Lett.* **2017**, *19*, 6514−6517. (c) Sheng, G. R.; Huang, K.; Chi, Z. H.; Ding, H. L.; Xing, Y. P.; Lu, P.; Wang, Y. G. Preparation of 3-Diazoindolin-2-imines *via* Cascade Reaction Between Indoles and Sulfonylazides and Their Extensions to 2,3-Diaminoindoles and Imidazo[4,5-*b*]indoles. *Org. Lett.* **2014**, *16*, 5096−5099.
(16) (a) Suleman, M.; Lu, P.; Wang, Y. G. Recent Advances in the Synthesis of Indole Embedded Heterocycles with 3-Diazoindolin-2-imines. *Org. Chem. Front.* **2021**, *8*, 2059−2078. (b) Lin, Z. W.; Qian, J.; Lu, P.; Wang, Y. G. Syntheses of 2-Iminoindolin-3-ones and 2-Alknyl-2,3-dihydroquinazolin-4(1*H*)-ones from 3-Diazoindolin-2-imines. *J. Org. Chem.* **2020**, *85*, 11766−11777. (c) Sheng, G. R.; Li, Z. M.; Mao, J. M.; Lu, P.; Wang, Y. G. General Approach To Construct Azepino[2,3-*b*:4,5-*b*′]diindoles, Azocino[2,3-*b*:4,5-*b*′]-diindoles, and Azonino[2,3-*b*:4,5-*b*′]diindoles *via* Rh(II)-Catalyzed Reactions of 3-Diazoindolin-2-imines with 3-(Bromoalkyl)indoles. *J. Org. Chem.* **2019**, *84*, 9561−9569.
(17) (a) Boddy, A. J.; Bull, J. A. Stereoselective Synthesis and Applications of Spirocyclic Oxindoles. *Org. Chem. Front.* **2021**, *8*, 1026−1084. (b) Sakla, A. P.; Kansal, P.; Shankaraiah, N. Syntheses and Applications of Spirocyclopropyl Oxindoles: A Decade Review. *Eur. J. Org. Chem.* **2021**, *2021*, 757−772. (c) Han, C. F.; Wu, W. J.; Chen, Z. Y.; Pu, S. Z. Rh-Catalyzed [5+1]-Cycloaddition Reactions to Spirobenzo[*e*][1,3]oxazineindoline Imines. *Asian J. Org. Chem.* **2019**, *8*, 1385−1389.
(18) Sheng, G. R.; Ma, S. C.; Bai, S. L.; Mao, J. M.; Lu, P.; Wang, Y. G. A Copper-Catalyzed Reaction of 3-Diazoindolin-2-imines with 2-(Phenylamino)ethanols: Convenient Access to Spiro[indoline-3,2'-oxazolidin]-2-imines. *Chem. Commun.* **2018**, *54*, 1529−1532.
(19) (a) Lou, J.; Ma, J.; Xu, B.-H.; Zhou, Y.-G.; Yu, Z. K. Photoinduced, Copper-Catalyzed Three-Component Annulation of *gem*-Dialkylthio Enynes. *Org. Lett.* **2020**, *22*, 5202−5206. (b) Xu, C.; Wang, M.; Liu, Q. Recent Advances in Metal-Catalyzed Bond-Forming Reactions of Ketene *S*,*S*-Acetals. *Adv. Synth. Catal.* **2019**, *361*, 1208−1229. (c) Zhang, L.; Dong, J. H.; Xu, X. X.; Liu, Q. Chemistry of Ketene *N*,*S*-Acetals: An Overview. *Chem. Rev.* **2016**, *116*, 287−322.
(20) (a) He, Y.; Lou, J.; Wu, P.; Zhou, Y.-G.; Yu, Z. K. Copper-Catalyzed Annulative Coupling of *S*,*S*-Disubstituted Enones with Diazo Compounds to Access Highly Functionalized Thiophene Derivatives. *J. Org. Chem.* **2020**, *85*, 1044−1053. (b) Liu, Z. Q.; Wu, P.; He, Y.; Yang, T.; Yu, Z. K. [4+1] Cycloaddition of Enaminothiones and Aldehyde *N*-Tosylhydrazones Toward 3-Aminothiophenes. *Adv. Synth. Catal.* **2018**, *360*, 4381−4392.
(21) Huang, F.; Liu, Z. Q.; Wang, Q. N.; Lou, J.; Yu, Z. K. Copper-Catalyzed Formal Carbene Migratory Insertion into Internal Olefinic C=C Bonds with *N*-Tosylhydrazones To Access Iminofuran and 2(3*H*)-Furanone Derivatives. *Org. Lett.* **2017**, *19*, 3660−3663.
(22) He, Y.; Lou, J.; Zhou, Y.-G.; Yu, Z. K. $ZnCl_2$-Catalyzed [4+1] Annulation of Alkylthio-Substituted Enaminones and Enaminothiones with Sulfur Ylides. *Chem.-Eur. J.* **2020**, *26*, 4941−4946.

https://doi.org/10.1021/acs.joc.2c00137
J. Org. Chem. 2022, 87, 4424−4437