JOC The Journal of Organic Chemistry

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Radical Deaminative *ipso*-Cyclization of 4-Methoxyanilines with 1,7-Enynes for Accessing Spirocyclohexadienone-Containing Cyclopenta[*c*]quinolin-4-ones

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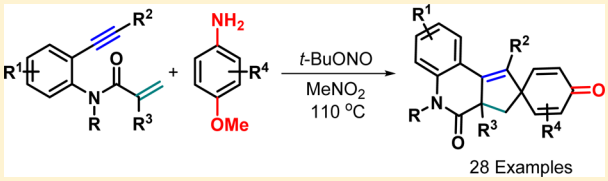
Supporting Information

ABSTRACT: A new C-center radical-triggered bicyclization cascade of *N*-tethered 1,7-enynes for forming 28 examples of biologically interesting spirocyclohexadienone-containing cyclopenta[*c*]quinolin-4-ones with two all-carbon quaternary stereocenters has been established under mild conditions. The in situ generated diazonium salts from 4-methoxyanilines and *t*-BuONO are served as 4-methoxyphenyl precursors without additional oxidant, enabling 6-*exo*-*dig* cyclization/5-*exo*-*trig* *ipso*-cyclization to construct three new C−C bonds through metal-free dearomatization. The reaction also features broad substrate scope, annulation efficiency, and high functional group tolerance.



INTRODUCTION

Spirocyclohexadienones appear as a pivotal core unit that exist in a myriad of natural products, such as spirobacillene A, stepharine, pronuciferine, and annosqualine (Figure 1), which

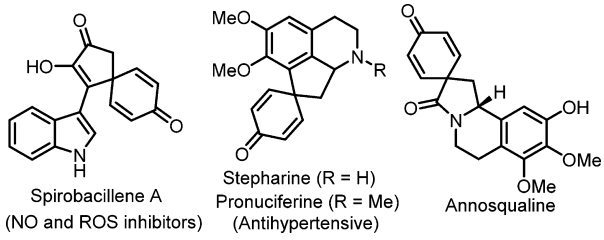


Figure 1. Some bioactive spirocyclohexadienone alkaloids.

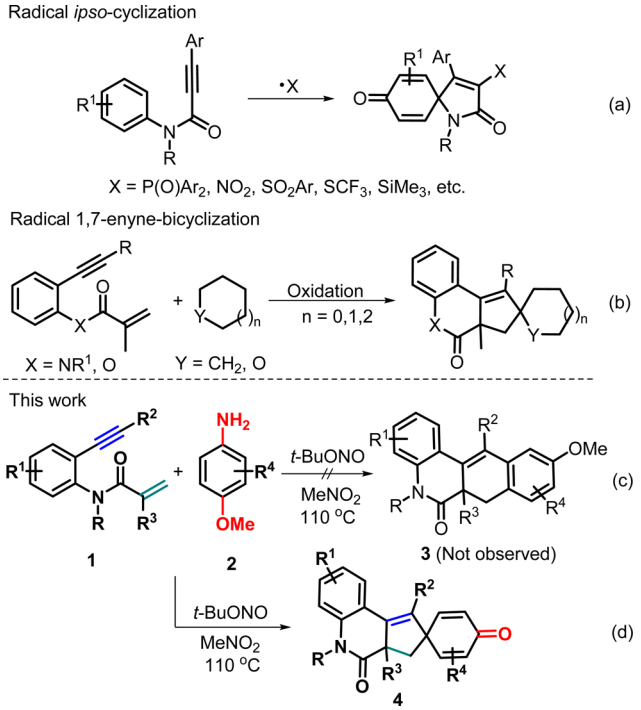
have been found to display a broad spectrum of biological activities.[1] Furthermore, spirocyclohexadienones are key intermediates in the synthesis of important alkaloids and related products.[2] With these attributes in mind, a great deal of effort aimed toward identifying general methods for the synthesis of these spirocyclohexadienones and their structural analogues has been made.[3] Generally, strategies for spirocyclohexadienone syntheses would be classified into four types, that is, oxidative dearomatization of phenols,[4] nitrenium-ion induced dearomatization[5] and intramolecular electrophilic *ipso*-spiroannulation[6] as well as radical-triggred *ipso*-spirocyclization.[7] Among them, the last provides an efficient and straightforward access to molecules containing spirocyclohexadienone motif with good functional group compatibility, especially well-developed oxidative difunctionalization of alkyne and thus has attracted the interest of synthetic chemists. For instance, several groups reported *ipso*-cyclization and dearomatization of *N*-arylpropiolamides to generate functionalized spirocyclohexadienones by using various radicals (Scheme 1a).[8] Despite these significant advances, however, radical deaminative *ipso*-cyclization of 4-methoxyanilines with 1,7-enynes for the construction of functionalized cyclopenta[*c*]-quinolin-4-ones bearing spirocyclohexadienone unit, to the best of our knowledge, is virtually unexplored.

Meanwhile, oxidative radical 1,7-enyne-bicyclization become a powerful and applicable methodology for the collection of polycyclic structures with all-carbon quaternary stereocenters via synergistic effect across the C═C and C≡C bond π system, with the advantage of atom economy and extreme convergence.[9] Besides, these reactions feature annulation efficiency and structural diversity and complexity without the isolation and purity of intermediates, thereby minimizing waste generation.[10] Recently, we and Li's group independently reported the addition of various C-centered radicals to benzene-tethered 1,7-enynes to generate spiro-fused compounds (Scheme 1b).[11] During this project, we reasoned that under a set of suitable conditions the preformed *N*-tethered 1,7-enynes **1** would capture aryl radicals generated *in situ* from the reaction of aryl amines **2** with *tert*-butyl nitrite,[12] followed by 6-*exo*-*dig*/6-*endo*-*trig* bicyclization to generate the desired tetracyclic benzo[*j*]phenanthridines **3** described by Li's group

Received: March 25, 2017
Published: June 8, 2017

DOI: 10.1021/acs.joc.7b00704
J. Org. Chem. 2017, 82, 6621−6628

Scheme 1. Profiling Applications of *ipso*-Cyclization

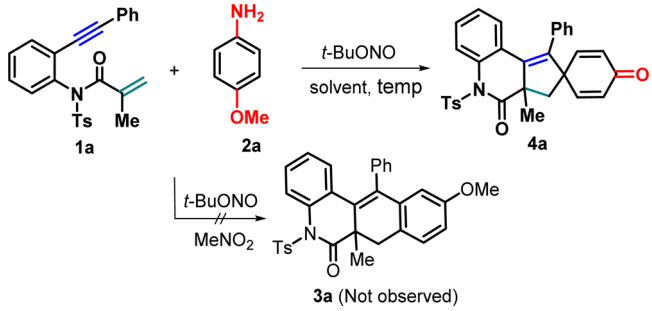


(Scheme 1c).[13] Interestingly, instead of the expected benzo[*j*]phenanthridine product **3**, this transformation proceeded in an unexpected 6-*exo*-*dig* cyclization/5-*exo*-*trig* *ipso*-cyclization direction, enabling radical-triggered dearomatization of 4-methoxyanilines to access tetracyclic spirocyclohexadienone-containing cyclopenta[*c*]quinolin-4-ones **4** with two quaternary stereocenters (Scheme 1d). Herein, we would like to report this attractive transformation. Note that this is the first site-selective radical-induced deamination and demethylation of 4-methoxyanilines for the creation of these significant polycyclic spirocyclohexadienones through a metal- and oxidant-free bicyclization cascade.

RESULTS AND DISCUSSION

To confirm the possibility of our designed method, commercially available 4-methoxyaniline was selected as a aryl radical source, due to arylamines being easily converted into the corresponding aryl radicals in the presence of *t*-butyl nitrite (*t*-BuONO).[12] Our initial investigation commenced with the reaction of the preformed *N*-Ts tethered 1,7-enyne **1a** with 4-methoxyaniline **2a** in a 1:5 mol ratio using *t*-BuONO as a deaminative reagent. The reaction was conducted in $MeNO_2$ solvent at 110 °C under air conditions, and the unexpected product **4a** was obtained in 39% yield without observation of the target product **3a** (Table 1, entry 1). This interesting result promoted us to search the optimal conditions for accessing product **4a**. Decreasing the mole ratio of **1a**:**2a** to 1:4 was adverse to this transformation and afforded a lower 30% yield (entry 2). The similar inferior outcome was observed by fine-tuning the ratio of **1a** with **2a** to 1:6 mol ratio (entry 3). Afterward, we considered to change the dosage of *t*-BuONO to improve the conversion of this bicyclization reaction. It was found that the increase of the dosage of *t*-BuONO is beneficial to the transformation (entries 4−5). The product **4a** was provided in a 51% yield when 10.0 equiv of *t*-BuONO were employed as a deaminating reagent (entry 5). As the next

Table 1. Optimization of Reaction Conditions for Forming Product 4a[a]



entry	**1a**:**2a** ratio	solvent	*T* (°C)	yield[b] (%)
1[c]	1:5	$MeNO_2$	110	39
2[c]	1:4	$MeNO_2$	110	30
3[c]	1:6	$MeNO_2$	110	35
4[d]	1:5	$MeNO_2$	110	42
5[e]	1:5	$MeNO_2$	110	51
6[e]	1:5	$MeNO_2$	80	trace
7[e]	1:5	$MeNO_2$	100	18
8[e]	1:5	$MeNO_2$	120	38
9[e]	1:5	$MeNO_2/H_2O$ (1:1)	110	35
10[e]	1:5	DMF	110	N.R.
11[e]	1:5	toluene	110	N.R.
12[e]	1:5	MeCN	110	N.R.
13[e]	1:5	DCM	110	trace
14[e]	1:5	DCE	110	trace

[a]Reaction condition: **1a** (0.2 mmol), **2** (x mmol), *t*-BuONO (y equiv), solvent (5.0 mL), air conditions. [b]Isolated yield based on substrate **1a**. [c]*t*-BuONO (5.0 equiv). [d]*t*-BuONO (8.0 equiv). [e]*t*-BuONO (10.0 equiv).

optimization step, we performed the screening of reaction temperature and reaction media. With the reaction temperature being at 80 °C, the deaminative bicyclization reaction hardly proceeded to give the desired product, suggesting that the reaction temperature critically affected the efficiency of the reaction (entry 6). The relatively lower conversion into **4a** was detected when the reaction was performed at either 100 or 120 °C (entries 7−8). The investigation of solvent effect revealed that the mixed solvent of $MeNO_2$−H_2O led to a lower conversion (entry 9) whereas the reaction did not work and the starting materials were recovered when *N*,*N*-dimethylformamide (DMF), toluene, or acetonitrile (MeCN) was selected as reaction media (entries 10−12). Similarly, the use of dichloromethane (DCM) and 1,2-dichloroethane (DCE) completely suppressed the reaction process (entries 13−14).

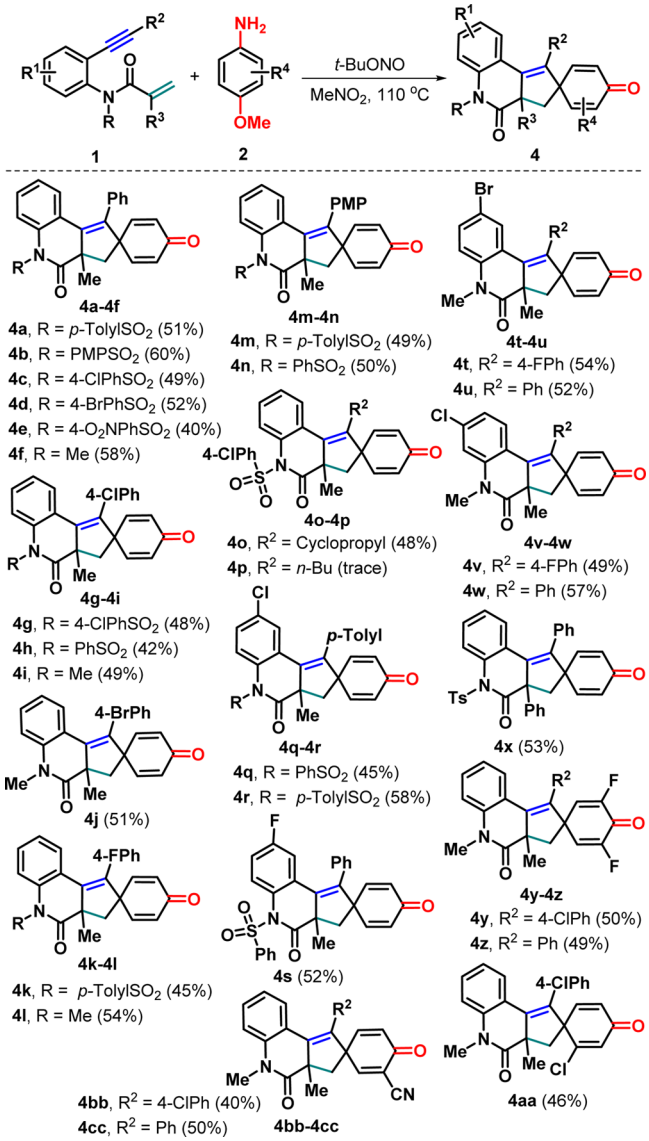
After determining the optimal reaction conditions (Table 1, entry 5), the generality of this metal-free oxidative bicyclization was investigate by examining *N*-tethered 1,7-enyne and 4-methoxyaniline components. At first, 1,7-enynes with diverse functionalities were investigated in combination with 4-methoxyaniline. With the phenyl ring (R^2) tethered by the alkynyl moiety, various substituents with electronically poor and rich nature at *para*-position of arylsulfonyl (R) moiety were proven not to hamper this radical-induced deamination, affording the corresponding spiro-fused cyclopenta[*c*]-quinolin-4-ones **4a**−**4e** in acceptable yields. Functional groups like methyl, methoxy chloride, bromide, and nitro were compatible with the deaminative conditions. Among them, a slight increase in the yield was obtained (**4b**, 60%) as the *p*-

DOI: 10.1021/acs.joc.7b00704
J. Org. Chem. 2017, 82, 6621−6628

methoxyphenyl (PMP) counterpart (**1b**) was served as a reaction partner whereas nitro group resulted in a significantly dropped yield (**4e**). Besides, *N*-methyl protected 1,7-enyne **1f** still showed high reactivity in current oxidative bicyclization, giving access to the corresponding product **4f** in 58% isolated yield. Next, electronic nature of substituents on the arylalkynyl (R^2) moiety was then explored by changing *N*-protected functionalities. As we had expected, the reaction proceeded readily with a variety of functional groups on both arylalkynyl and *N*-protected moieties of substrates **1**, leading to the assembly of structurally diverse cyclopenta[*c*]quinolin-4-one products **4g**–**4n** in moderate yields. Alternatively, substrate **1o** with a cyclopropyl group on the alkynyl moiety was proven to be a suitable radical precursor, providing the corresponding product **4o** in 48% yield. Unluckily, *n*-butyl (*n*-Bu) counterpart **1p** was not an adaptable candidate, as the reaction only gave a trace amount of product **4p** failed to be isolated. Afterward, the substrates **1** bearing chloro, fluoro, and bromo groups at 4- or 5-position of the internal arene ring were successfully engaged in the current radical *ipso*-annulation, delivering the corresponding spirocyclic cyclopenta[*c*]quinolin-4-ones **4q**–**4w** with yields ranging from 45 to 58%. Replacing methyl group with a phenyl ring on the terminal olefin unit, 1,7-conjugated enyne **1x** would be accommodated, enabling 6-*exo*-*dig*/5-*exo*-*trig* bicyclization, rather than 6-*exo*-*dig*/5-*endo*-*trig* bicyclization reported by Wang et al.,[14] under the standard conditions to access the corresponding **4x** in 53% yield. In view of these results, we considered exploiting 4-methoxyanilines with diverse substituents to explore the feasibility of the reaction and selected 3,5-difluoro, 2-chloro, and 3-cyano counterparts as representative deaminative coupling partners. As anticipated, this metal-free radical strategy tolerates various functional groups like fluoride, chloride, and cyano at different positions on the 4-methoxyaniline ring, furnishing the corresponding spiro-fused cyclopenta[*c*]quinolin-4-ones **4y**-**4** **cm**[3] with structural diversity, albeit with 40–50% yield (Scheme 2). It is noteworthy that the current protocol represents a new and practical pathway for the construction of richly decorated fused cyclopenta[*c*]quinolin-4-ones **4**, which are normally difficult to synthesize by other methods.[10] The structures of these cyclopenta[*c*]quinolin-4-ones **4** were characterized by their NMR spectroscopy and HRMS. In the case of **4h**, its structure was unequivocally confirmed by carrying out single crystal X-ray diffraction (see Supporting Information).[15]

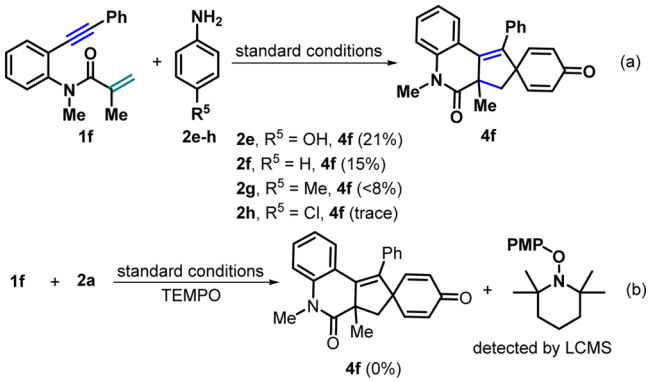
To understand this reaction mechanism, the following control experiments were carried out. *N*-Tethered 1,7-enyne **1f** was subjected to the reaction with aryl amines with substituents including OH (**2e**), H (**2f**), Me (**2g**), and Cl (**2h**) at its *para*-position, respectively. Very low conversion was obtained when either arylamine **2e**, **2f**, or **2g** behaved as an *ipso*-cyclization candidate whereas only trace amount of the desired product **4f** was detected with use of 4-chloro counterpart (Scheme 3a). These experimental outcomes indicated that the methoxy group at *para*-position of phenyl ring is beneficial to the present transformation. After that, 10.0 equiv of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) as a radical scavenger was added into the reaction system under standard conditions, but no product **4f** was generated with the starting material **1f** remaining (Scheme 3b). For this reaction, the TEMPO–PMP adduct was detected by LC-MS (MS = 263.2) analysis, suggesting that the deaminative bicyclization reaction may be involved in a free-radical process, consistent with the literature precedents of *t*-BuONO-mediated deamination.[12]

Scheme 2. Domino Synthesis of Products 4[a]



[a]Reaction conditions: All reactions were performed with **1** (0.2 mmol), **2** (1.0 mmol), *t*-BuONO (2.0 mmol), and $MeNO_2$ (5.0 mL) at 110 °C under air conditions for 12 h. [b]Isolated yield based on **1**.

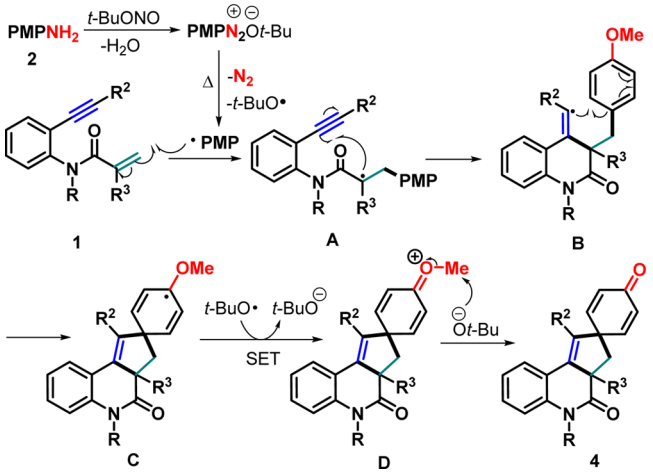
Scheme 3. Control Experiments



DOI: 10.1021/acs.joc.7b00704
J. Org. Chem. 2017, 82, 6621–6628

Combining our own observations and literature survey,[10,12] we proposed a reasonable radical-triggered mechanism as shown in Scheme 4. The first step is to form 4-

Scheme 4. Proposed Mechanism for Forming Products 4



methoxyphenyldiazonium ion, generated in situ from anilines and *t*-BuONO,[12] which gives the PMP radical by decomposition of itself with concurrent releasing of N_2 and *t*-butoxyl radical (*t*-BuO·) under heating conditions.[16] Subsequently, the resulting PMP radical added to the terminal alkene unit of 1,7-enynes **1**, followed by 6-*exo*-*dig* /5-*exo*-*trig* bicyclization to give the radical intermediate **C**. Next, single electron transfer (SET) oxidation between **C** and *t*-butoxyl radical occurs to access oxygenium intermediate **D**, which is converted into the final products **4** in the presence of bases through demethylation.[17]

In conclusion, we have established a new C-center radical-triggered bicyclization of *N*-tethered 1,7-enynes with a large variety of functional groups, by which a broad range of spirocyclohexadienone-containing cyclopenta[*c*]quinolin-4-ones with two all-carbon quaternary stereocenters would be synthesized through *t*-BuONO-mediated deaminative *ipso*-cyclization under oxidant-free conditions. This reaction proceeds through key methine radical species formed by addition of PMP radicals to *N*-tethered 1,7-enynes, resulting in multiple C−C bond-forming events with the concomitant cleavage of C−N and C−O of 4-methoxyanilines under oxidative conditions. The bond-forming/annulation efficiency and functional group tolerance make this metal-free transformation a direct and powerful synthetic tool with a great substrate scope. Further investigation on the mechanistic insight is underway in our laboratory.

EXPERIMENTAL SECTION

General Information. All melting points are uncorrected. The NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 on a 400 MHz instrument with TMS as internal standard. Chemical shifts (δ) were reported in ppm with respect to TMS. Data are represented as follows: chemical shift, mutiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constant (J, Hz), and integration. HRMS analyses were carried out using a TOF-MS instrument with an ESI source. X-ray crystallographic analysis was performed with a SMART CCD and a P4 diffractometer.

General Procedure for the Synthesis of 4. *Example for the Synthesis of* ***4a****.* *N*-(2-(Phenylethynyl)phenyl)-*N*-tosylmethacrylamide (**1a**, 83.2 mg, 0.2 mmol 1.0 equiv), 4-methoxyaniline (**2a**, 123 mg, 1.0 mmol 5.0 equiv), *t*-BuONO (206 mg, 2.0 mmol 10.0 equiv), and $MeNO_2$ (5.0 mL) were successively added in a 25 mL reaction vial under air conditions. The reaction vial was sealed and stirred at 110 °C for 12 h until TLC (petroleum ether:ethyl acetate = 1:2) revealed that conversion of the starting material **1a** was completed. Then the reaction mixture was extracted with ethyl acetate and was concentrated in vacuo. After that, the crude product was purified by flash column chromatography (silica gel, petroleum ether/acetic ester) to afford the desired pure product **4a**.

3a′-Methyl-1′-phenyl-5′-tosyl-3′,3a′-dihydrospiro[cyclohexa-[2,5]diene-1,2′-cyclopenta[c]quinoline]-4,4′(5′H)-dione (***4a***). Orange solid, 51.7 mg, 51% yield; mp 236−237 °C; IR (KBr, ν, cm^{-1}) 2971, 1721, 1666, 1540, 1475, 1372, 1247, 1171, 814, 779; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.84 (d, J = 8.4 Hz, 2H), 7.72 (d, J = 8.0 Hz, 1H), 7.53 (d, J = 8.4 Hz, 2H), 7.45−7.41 (m, 1H), 7.36−7.33 (m, 4H), 7.20−7.16 (m, 1H), 7.07−7.05 (m, 2H), 6.84 (d, J = 7.6 Hz, 1H), 6.22 (d, J = 10.0 Hz, 1H), 5.94−5.88 (m, 2H), 2.46−2.42 (m, 4H), 2.20 (d, J = 14.4 Hz, 1H), 1.22 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 184.7, 174.7, 153.4, 152.5, 146.0, 140.6, 137.0, 136.1, 134.8, 133.5, 130.2, 129.0, 128.9, 128.8, 128.7, 128.6, 127.4, 127.2, 125.4, 125.0, 57.6, 56.6, 43.4, 24.0, 21.6; HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{31}H_{26}NO_4S$, 508.1583; Found 508.1572.

5′-((4-Methoxyphenyl)sulfonyl)-3a′-methyl-1′-phenyl-3′,3a′-dihydrospiro[cyclohexa[2,5]diene-1,2′-cyclopenta[c]quinoline]-4,4′(5′H)-dione (***4b***). Orange solid, 62.8 mg, 60% yield; mp 173−174 °C; IR (KBr, ν, cm^{-1}) 2971, 1719, 1667, 1540, 1456, 1371, 1266, 1167, 836, 795; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.90 (d, J = 9.2 Hz, 2H), 7.72 (d, J = 8.4 Hz, 1H), 7.45−7.41 (m, 1H), 7.36−7.32 (m, 4H), 7.23 (d, J = 8.8 Hz, 2H), 7.19−7.15 (m, 1H), 7.06−7.04 (m, 2H), 6.83 (d, J = 7.6 Hz, 1H), 6.23−6.21 (m, 1H), 5.96−5.93 (m, 1H), 5.88−5.85 (m, 1H), 3.88 (s, 3H), 2.47 (d, J = 14.0 Hz, 1H), 2.21 (d, J = 14.4 Hz, 1H), 1.21 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 184.7, 174.6, 164.3, 153.4, 152.6, 140.6, 137.1, 134.8, 133.5, 131.3, 130.1, 128.9(3), 128.9(0), 128.8(3), 128.8(0), 128.5, 127.3, 127.1, 125.4, 124.9, 114.9, 57.6, 56.6, 56.5, 43.4, 24.0; HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{31}H_{26}NO_5S$ 524.1532; Found 524.1515.

5′-((4-Chlorophenyl)sulfonyl)-3a′-methyl-1′-phenyl-3′,3a′-dihydrospiro[cyclohexa[2,5]diene-1,2′-cyclopenta[c]quinoline]-4,4′(5′H)-dione (***4c***). Orange solid, 51.7 mg, 49% yield; mp 198−199 °C; IR (KBr, ν, cm^{-1}) 2997, 1717, 1637, 1558, 1489, 1385, 1184, 1015, 862, 668; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.99 (d, J = 8.4 Hz, 2H), 7.82 (d, J = 8.8 Hz, 2H), 7.74 (d, J = 8.0 Hz, 1H), 7.46−7.43 (m, 1H), 7.37−7.33 (m, 4H), 7.22−7.18 (m, 1H), 7.07−7.05 (m, 2H), 6.85 (d, J = 7.6 Hz, 1H), 6.25−6.22 (m, 1H), 5.99−5.89 (m, 2H), 2.49 (d, J = 13.2 Hz, 1H), 2.23 (d, J = 14.4 Hz, 1H), 1.23 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 184.7, 174.7, 153.3, 152.4, 140.9, 140.2, 137.7, 136.7, 134.5, 133.5, 130.6, 130.0, 129.1, 128.9, 128.9, 128.8, 128.8, 128.7, 127.5, 127.4, 125.4, 124.8, 57.6, 56.5, 43.3, 23.9; HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{30}H_{23}NO_4SCl$ 528.1036; Found 528.1027.

5′-((4-Bromophenyl)sulfonyl)-3a′-methyl-1′-phenyl-3′,3a′-dihydrospiro[cyclohexa[2,5]diene-1,2′-cyclopenta[c]quinoline]-4,4′(5′H)-dione (***4d***). Orange solid, 59.4 mg, 52% yield; mp 179−181 °C; IR (KBr, ν, cm^{-1}) 2966, 1729, 1666, 1571, 1472, 1386, 1238, 1169, 860, 757; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.98−7.89 (m, 4H), 7.74 (d, J = 8.4 Hz, 1H), 7.46−7.42 (m, 1H), 7.36−7.33 (m, 4H), 7.22−7.18 (m, 1H), 7.06−7.05 (m, 2H), 6.85 (d, J = 7.6 Hz, 1H), 6.23 (d, J = 10.4 Hz, 1H), 5.95−5.89 (m, 2H), 2.49 (d, J = 12.4 Hz, 1H), 2.23 (d, J = 14.0 Hz, 1H), 1.23 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 184.6, 174.7, 153.3, 152.3, 140.9, 138.1, 136.7, 134.5, 133.4, 133.0, 130.6, 129.3, 129.1, 128.9(2), 128.9(0), 128.8(4), 128.8(0), 128.6, 127.5, 127.4, 125.4, 124.9, 57.6, 56.5, 43.3, 23.9; HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{30}H_{23}NO_4SBr$ 572.0531; Found 572.0525.

3a′-Methyl-5′-((4-nitrophenyl)sulfonyl)-1′-phenyl-3′,3a′-dihydrospiro[cyclohexa[2,5]diene-1,2′-cyclopenta[c]quinoline]-4,4′(5′H)-dione (***4e***). Orange solid, 43.0 mg, 40% yield; mp 224−225 °C; IR (KBr, ν, cm^{-1}) 2975, 1723, 1664, 1538, 1456, 1375, 1233, 1174, 1084, 857; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.02 (d, J = 8.0 Hz, 2H), 7.81 (d, J = 8.4 Hz, 1H), 7.70−7.66 (m, 1H), 7.58−7.55 (m, 2H), 7.41−7.37 (m, 1H), 7.22 (d, J = 8.4 Hz, 2H), 7.14−7.10 (m,

DOI: 10.1021/acs.joc.7b00704
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1H), 7.04−6.99 (m, 3H), 6.91 (d, J = 7.6 Hz, 1H), 6.33 (d, J = 9.6 Hz, 1H), 6.01−5.92 (m, 2H), 2.64 (d, J = 14.8 Hz, 1H), 2.10 (d, J = 14.4 Hz, 1H), 1.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 184.9, 174.9, 152.1, 151.8, 150.7, 145.2, 140.9, 136.4, 134.5, 133.1, 129.8, 129.4, 129.2, 129.0, 128.9, 128.7, 128.1, 128.0, 127.0, 124.8, 124.1, 123.7, 57.3, 56.3, 44.3, 24.1; HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{30}H_{23}N_2O_6S$ 539.1277; Found 539.1282.

3a′,5′-Dimethyl-1′-phenyl-3′,3a′-dihydrospiro[cyclohexa[2,5]-diene-1,2′-cyclopenta[c]quinoline]-4,4′(5′H)-dione (**4f**). Orange solid, 42.6 mg, 58% yield; mp 200−202 °C; IR (KBr, ν, cm^{-1}) 2976, 1716, 1647, 1540, 1472, 1387, 1280, 1123, 867, 772; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.47−7.44 (m, 1H), 7.33−7.23 (m, 5H), 7.08−7.06 (m, 2H), 6.95−6.91 (m, 1H), 6.84−6.80 (m, 1H), 6.72 (d, J = 6.4 Hz, 1H), 6.28−6.25 (m, 1H), 5.99−5.96 (m, 1H), 3.37 (s, 3H), 2.90 (d, J = 14.0 Hz, 1H), 2.21 (d, J = 14.0 Hz, 1H), 1.39 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 185.1, 174.0, 154.7, 154.2, 140.1, 138.8, 138.7, 135.0, 129.9, 128.8, 128.7, 128.6, 128.4(3), 128.4(0), 127.4, 122.8, 120.5, 116.2, 57.5, 53.5, 44.2, 30.1, 26.1; HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{25}H_{22}NO_2$ 368.1651; Found 368.1641.

1′-(4-Chlorophenyl)-5′-((4-chlorophenyl)sulfonyl)-3a′-methyl-3′,3a′-dihydrospiro[cyclohexa[2,5]diene-1,2′-cyclopenta[c]-quinoline]-4,4′(5′H)-dione (**4g**). Orange solid, 53.9 mg, 48% yield; mp 199−200 °C; IR (KBr, ν, cm^{-1}) 2989, 1718, 1662, 1540, 1473, 1385, 1174, 1043, 863, 756; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 8.00 (d, J = 8.8 Hz, 2H), 7.82 (d, J = 8.4 Hz, 2H), 7.75 (d, J = 8.0 Hz, 1H), 7.49−7.45 (m, 1H), 7.42 (d, J = 8.4 Hz, 2H), 7.37−7.34 (m, 1H), 7.26−7.22 (m, 1H), 7.08 (d, J = 8.4 Hz, 2H), 6.88 (d, J = 7.2 Hz, 1H), 6.25 (d, J = 10.0 Hz, 1H), 5.98−5.91 (m, 2H), 2.49 (d, J = 14.4 Hz, 1H) 2.23 (d, J = 14.0 Hz, 1H), 1.23 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 184.6, 174.6, 153.1, 152.2, 140.2, 139.4, 137.7, 137.4, 134.5, 133.7, 132.3, 130.7, 130.6, 130.1, 129.3, 129.1, 120.0, 128.8, 127.5, 125.1, 124.9, 57.5, 56.6, 43.3, 23.9; HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{30}H_{22}NO_4SCl_2$ 562.0647; Found 562.0652.

1′-(4-Chlorophenyl)-3a′-methyl-5′-(phenylsulfonyl)-3′,3a′-dihydrospiro[cyclohexa[2,5]diene-1,2′-cyclopenta[c]quinoline]-4,4′(5′H)-dione (**4h**). Orange solid, 44.3 mg, 42% yield; mp 271−273 °C; IR (KBr, ν, cm^{-1}) 2977, 1718, 1663, 1596, 1453, 1347, 1246, 1171, 1085, 862; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.00 (d, J = 8.0 Hz, 2H), 7.79−7.76 (m, 1H), 7.70−7.67 (m, 1H), 7.59−7.55 (m, 2H), 7.31−7.26 (m, 3H), 7.10−7.05 (m, 1H), 7.02−6.99 (m, 3H), 6.60−6.57 (m, 1H), 6.31 (d, J = 10.0 Hz, 1H), 5.95 (d, J = 10.0 Hz, 1H), 5.86−5.83 (m, 1H), 2.62 (d, J = 14.8 Hz, 1H), 2.09 (d, J = 14.8 Hz, 1H), 1.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 184.8, 174.4, 152.1, 151.7, 139.4, 138.7, 138.0, 135.0, 134.8, 134.0, 131.7, 129.5, 129.3, 129.2, 128.9, 128.8, 128.6, 127.4, 126.8, 124.7, 124.6, 57.2, 56.6, 44.2, 24.1; HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{30}H_{23}NO_4SCl$ 528.1036; Found 528.1037.

1′-(4-Chlorophenyl)-3a′,5′-dimethyl-3′,3a′-dihydrospiro-[cyclohexa[2,5]diene-1,2′-cyclopenta[c]quinoline]-4,4′(5′H)-dione (**4i**). Orange solid, 39.3 mg, 49% yield; mp 202−204 °C; IR (KBr, ν, cm^{-1}) 2945, 1716, 1663, 1540, 1472, 1387, 1282, 1175, 862,752; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.46−7.43 (m, 1H), 7.37−7.31 (m, 3H), 7.25 (d, J = 8.4 Hz, 1H), 7.09 (d, J = 8.4 Hz, 2H), 6.94−6.91 (m, 1H), 6.90−6.86 (m, 1H), 6.75 (d, J = 7.6 Hz, 1H), 6.28−6.25 (m, 1H), 6.02−5.99 (m, 1H), 3.37 (s, 3H), 2.90 (d, J = 14.0 Hz, 1H), 2.20 (d, J = 14.0 Hz, 1H), 1.39 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 185.0, 173.9, 154.5, 154.0, 140.2, 139.5, 137.3, 133.9, 133.1, 130.6, 130.1, 129.0, 128.7, 128.5, 127.4, 122.9, 120.2, 116.3, 57.3, 53.6, 44.2, 30.1, 26.1; HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{25}H_{21}NO_2Cl$ 402.1261; Found 402.1252.

1′-(4-Bromophenyl)-3a′,5′-dimethyl-3′,3a′-dihydrospiro-[cyclohexa[2,5]diene-1,2′-cyclopenta[c]quinoline]-4,4′(5′H)-dione (**4j**). Orange solid, 45.4 mg, 51% yield; mp 191−192 °C; IR (KBr, ν, cm^{-1}) 3127, 1663, 1601, 1460, 1401, 1350, 1281, 1175, 1008, 862; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.46−7.43 (m, 1H), 7.34−7.30 (m, 1H), 7.24 (d, J = 8.0 Hz, 1H), 7.16−7.10 (m, 4H), 6.95−6.92 (m, 1H), 6.88−6.84 (m, 1H), 6.74−6.72 (m, 1H), 6.28−6.25 (m, 1H), 6.01−5.98 (m, 1H), 3.37 (s, 3H), 2.89 (d, J = 14.0 Hz, 1H), 2.20 (d, J = 14.0 Hz, 1H), 1.38 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 185.0, 173.9, 154.5, 154.1, 140.1, 139.5, 137.3, 134.3, 131.9, 130.9, 130.1, 128.7, 128.5, 127.4, 122.9, 121.8, 120.2, 116.3, 57.3, 53.6, 44.2, 30.1, 26.0; HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{25}H_{21}NO_2Br$ 446.0756; Found 446.0757.

1′-(4-Fluorophenyl)-3a′-methyl-5′-tosyl-3′,3a′-dihydrospiro-[cyclohexa[2,5]diene-1,2′-cyclopenta[c]quinoline]-4,4′(5′H)-dione (**4k**). Orange solid, 47.3 mg, 45% yield; mp 236−237 °C; IR (KBr, ν, cm^{-1}) 2980, 1722, 1659, 1540, 1457, 1367, 1219, 1173, 817, 788; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.84 (d, J = 8.4 Hz, 2H), 7.73 (d, J = 8.0 Hz, 1H), 7.52 (d, J = 8.4 Hz, 2H), 7.47−7.43 (m, 1H), 7.36−7.33 (m, 1H), 7.24−7.17 (m, 3H), 7.12−7.08 (m, 2H), 6.86 (d, J = 7.6 Hz, 1H), 6.23 (d, J = 10.0 Hz, 1H), 5.93−5.87 (m, 2H), 2.46−2.42 (m, 4H), 2.19 (d, J = 14.0 Hz, 1H), 1.21 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 184.6, 174.6, 162.4 ($^1J_{CF}$ = 244.3 Hz), 153.3, 152.3, 146.0, 139.4, 137.4, 136.1, 134.8, 131.0 ($^3J_{CF}$ = 8.3 Hz), 130.2, 129.8 ($^4J_{CF}$ = 3.2 Hz), 129.1, 128.9, 128.7(2), 128.7(0), 127.4, 127.3, 125.2, 125.0, 116.0 ($^2J_{CF}$ = 21.4 Hz), 57.5, 56.6, 43.3, 23.9, 21.6; HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{31}H_{25}NO_4SF$ 526.1488; Found 526.1475.

1′-(4-Fluorophenyl)-3a′,5′-dimethyl-3′,3a′-dihydrospiro-[cyclohexa[2,5]diene-1,2′-cyclopenta[c]quinoline]-4,4′(5′H)-dione (**4l**). Orange solid, 41.6 mg, 54% yield; mp 118−119 °C; IR (KBr, ν, cm^{-1}) 3127, 1662, 1600, 1557, 1506, 1401, 1223, 1174, 1106, 836; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.49 (d, J = 8.4 Hz, 2H), 7.46−7.43 (m, 1H), 7.35−7.31 (m, 1H), 7.25 (d, J = 8.4 Hz, 1H), 7.03 (d, J = 8.4 Hz, 2H), 6.94−6.86 (m, 2H), 6.76−6.74 (m, 1H), 6.28−6.25 (m,1H), 6.02−5.99 (m, 1H), 3.35 (s, 3H), 2.89 (d, J = 14.0 Hz, 1H), 2.20 (d, J = 14.0 Hz, 1H), 1.38 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 185.0, 173.9, 154.6, 154.1, 140.1, 139.2, 137.6, 131.3 ($^4J_{CF}$ = 3.3 Hz), 130.9 ($^3J_{CF}$ = 8.1 Hz), 130.0, 128.7, 128.5, 127.4, 121.6 ($^1J_{CF}$ = 253.8 Hz), 116.2, 115.8 ($^2J_{CF}$ = 21.2 Hz), 57.4, 53.5, 44.1, 30.1, 26.1; HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{25}H_{21}NO_2F$ 386.1556; Found 386.1563.

1′-(4-Methoxyphenyl)-3a′-methyl-5′-tosyl-3′,3a′-dihydrospiro-[cyclohexa[2,5]diene-1,2′-cyclopenta[c]quinoline]-4,4′(5′H)-dione (**4m**). Orange solid, 52.6 mg, 49% yield; mp 173−174 °C; IR (KBr, ν, cm^{-1}) 2931, 1717, 1635, 1540, 1473, 1366, 1250, 1170, 810, 766; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.82 (d, J = 8.4 Hz, 2H), 7.72 (d, J = 8.0 Hz, 1H), 7.51 (d, J = 8.0 Hz, 2H), 7.45−7.41 (m, 1H), 7.33 (d, J = 10.4 Hz, 1H), 7.23−7.19 (m, 1H), 6.99 (d, J = 8.4 Hz, 2H), 6.90 (d, J = 8.4 Hz, 3H), 6.23 (d, J = 9.6 Hz, 1H), 5.95−5.83 (m, 2H), 3.74 (s, 3H), 2.43 (s, 3H), 2.42 (d, J = 8.0 Hz, 1H), 2.16 (d, J = 14.0 Hz, 1H), 1.19 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 184.8, 174.7, 159.6, 153.7, 152.8, 145.9, 140.3, 136.2, 136.1, 134.8, 130.2, 130.0, 128.8, 128.7, 128.6(4), 128.6(0), 127.4, 127.3, 125.7, 125.5, 125.0, 114.3, 57.6, 56.4, 55.5, 43.4, 23.8, 21.6; HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{32}H_{28}NO_5S$ 538.1688; Found 538.1674.

1′-(4-Methoxyphenyl)-3a′-methyl-5′-(phenylsulfonyl)-3′,3a′-dihydrospiro[cyclohexa[2,5]diene-1,2′-cyclopenta[c]quinoline]-4,4′(5′H)-dione (**4n**). Orange solid, 52.3 mg, 50% yield; mp 191−192 °C; IR (KBr, ν, cm^{-1}) 2976, 1715, 1664, 1540, 1452, 1369, 1247, 1169, 862, 783; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.93 (d, J = 8.0 Hz, 2H), 7.85−7.82 (m, 1H), 7.74−7.69 (m, 3H), 7.47−7.43 (m, 1H), 7.34−7.31 (m, 1H), 7.24−7.21 (m, 1H), 6.99 (d, J = 8.8 Hz, 2H), 6.92−6.89 (m, 3H), 6.24−6.21 (m, 1H), 5.91−5.89 (m, 1H), 5.82−5.79 (m, 1H), 3.74 (s, 3H), 2.40 (d, J = 14.0 Hz, 1H), 2.16 (d, J = 14.0 Hz, 1H), 1.20 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 184.8, 174.7, 159.6, 153.7, 152.7, 140.4, 138.9, 136.0, 135.1, 134.7, 130.0, 129.8, 128.9, 128.7, 128.6(1), 128.6(0), 127.4(4), 127.4(0), 125.8, 125.5, 125.1, 114.3, 57.5, 56.4, 55.5, 43.4, 23.8; HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{31}H_{26}NO_5S$ 524.1532; Found 524.1528.

5′-((4-Chlorophenyl)sulfonyl)-1′-cyclopropyl-3a′-methyl-3′,3a′-dihydrospiro[cyclohexa[2,5]diene-1,2′-cyclopenta[c]quinoline]-4,4′(5′H)-dione (**4o**). Orange solid, 47.1 mg, 48% yield; mp 221−222 °C; IR (KBr, ν, cm^{-1}) 2995, 1710, 1658, 1562, 1489, 1370, 1208, 1163, 1005, 857; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 7.83−7.80 (m, 2H), 7.76−7.74 (m, 1H), 7.55−7.52 (m, 1H), 7.49−7.46 (m, 2H), 7.45−7.41 (m, 1H), 7.38−7.34 (m, 1H), 6.76−6.73 (m, 1H), 6.28−6.25 (m, 1H), 6.10−6.07 (m, 1H), 5.75−5.71 (m, 1H), 2.57 (d, J = 14.8 Hz, 1H), 1.90 (d, J = 14.8 Hz, 1H), 1.40−1.32 (m, 1H), 1.08 (s,

DOI: 10.1021/acs.joc.7b00704
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3H), 0.75−0.62 (m, 2H), 0.51−0.45 (m, 1H), 0.31−0.25 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 185.3, 174.4, 150.0, 152.2, 141.9, 140.7, 137.6, 135.3, 134.3, 130.1, 129.1, 129.0, 128.4, 128.2, 128.0, 126.8, 125.8, 124.6, 57.1, 56.1, 43.0, 23.8, 9.5, 8.9, 5.9; HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{27}H_{23}NO_4SCl$ 492.1036; Found 492.1022.

8′-Chloro-3a′-methyl-5′-(phenylsulfonyl)-1′-(p-tolyl)-3′,3a′-dihydrospiro[cyclohexa[2,5]diene-1,2′-cyclopenta[c]quinoline]-4,4′(5′H)-dione (**4q**). Orange solid, 48.7 mg, 45% yield; mp 205−206 °C; IR (KBr, ν, cm^{-1}) 2967, 1721, 1664, 1559, 1466, 1385, 1256, 1126, 882, 738; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.95 (d, J = 7.6 Hz, 2H), 7.87−7.83 (m, 1H), 7.77 (d, J = 8.8 Hz, 1H), 7.73−7.69 (m, 2H), 7.54−7.52 (m, 1H), 7.32−7.29 (m, 1H), 7.17 (d, J = 7.6 Hz, 2H), 6.95 (d, J = 8.0 Hz, 2H), 6.83 (d, J = 2.4 Hz, 1H), 6.23−6.21 (m, 1H), 5.91−5.88 (m, 1H), 5.80−5.77 (m, 1H), 2.40 (d, J = 14.0 Hz, 1H), 2.29 (s, 3H), 2.18 (d, J = 14.0 Hz, 1H), 1.23 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 184.7, 174.4, 153.2, 152.2, 142.4, 138.6, 135.3, 135.0, 133.6, 131.5, 130.0, 129.9, 129.6, 128.8(4), 128.8(0), 128.7(4), 128.7(0), 128.5, 127.5, 126.9, 126.8, 57.6, 56.3, 43.3, 23.7, 21.3; HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{31}H_{25}NO_4SCl$ 542.1193; Found 542.1180.

8′-Chloro-3a′-methyl-1′-(p-tolyl)-5′-tosyl-3′,3a′-dihydrospiro-[cyclohexa[2,5]diene-1,2′-cyclopenta[c]quinoline]-4,4′(5′H)-dione (**4r**). Orange solid, 64.4 mg, 58% yield; mp 215−216 °C; IR (KBr, ν, cm^{-1}) 2993, 1717, 1653, 1540, 1472, 1375, 1173, 1128, 820, 668; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.84 (d, J = 8.0 Hz, 2H), 7.75 (d, J = 8.8 Hz, 1H), 7.52 (d, J = 8.8 Hz, 3H), 7.33−7.29 (m, 1H), 7.17 (d, J = 8.0 Hz, 2H), 6.94 (d, J = 8.0 Hz, 2H), 6.82 (d, J = 2.4 Hz, 1H), 6.22 (d, J = 9.6 Hz, 1H), 5.91−5.84 (m, 2H), 2.44 (s, 3H), 2.43 (d, J = 10.0 Hz, 1H), 2.29 (s, 3H), 2.18 (d, J = 14.0 Hz, 1H), 1.23 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 184.7, 174.4, 153.2, 152.2, 146.2, 142.3, 138.6, 135.8, 135.2, 133.6, 131.4, 130.3, 130.0, 129.6, 128.8, 128.7(4), 128.7(0), 128.5, 127.5, 126.9, 126.7, 57.6, 56.3, 43.3, 23.8, 21.6, 21.3; HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{32}H_{27}NO_4SCl$ 556.1349; Found 556.1346.

8′-Fluoro-3a′-methyl-1′-phenyl-5′-(phenylsulfonyl)-3′,3a′-dihydrospiro[cyclohexa[2,5]diene-1,2′-cyclopenta[c]quinoline]-4,4′(5′H)-dione (**4s**). Orange solid, 53.1 mg, 52% yield; mp 236−237 °C; IR (KBr, ν, cm^{-1}) 3123, 1718, 1655, 1585, 1400, 1371, 1256, 1180, 1084, 854; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 8.41 (d, J = 8.4 Hz, 2H), 8.26 (d, J = 8.4 Hz, 2H), 7.78 (d, J = 8.4 Hz, 1H), 7.40−7.36 (m, 1H), 7.33−7.26 (m, 3H), 7.13−7.07 (m, 4H), 6.96 (d, J = 7.6 Hz, 1H), 6.36 (d, J = 10.0 Hz, 1H), 6.25−6.20 (m, 1H), 6.05 (d, J = 10.0 Hz, 1H), 2.70 (d, J = 14.4 Hz, 1H), 2.15 (d, J = 14.8 Hz, 1H), 1.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 184.9, 174.2, 160.6 ($^1J_{CF}$ = 247.2 Hz), 151.8, 151.5, 141.8, 139.1, 136.3(9), 136.3(7), 134.1, 132.6, 131.0 ($^4J_{CF}$ = 3.1 Hz), 129.3, 129.1, 129.0, 128.9, 128.7(0), 128.6(7), 128.0, 127.1, 127.0, 126.5 ($^3J_{CF}$ = 8.6 Hz), 115.8, 115.6, 114.1 ($^2J_{CF}$ = 23.9 Hz), 57.4, 56.4, 44.1, 24.1; HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{30}H_{23}NO_4SF$ 512.1332; Found 512.1333.

8′-Bromo-1′-(4-fluorophenyl)-3a′,5′-dimethyl-3′,3a′-dihydrospiro[cyclohexa[2,5]diene-1,2′-cyclopenta[c]quinoline]-4,4′(5′H)-dione (**4t**). Orange solid, 50.0 mg, 54% yield; mp 125−127 °C; IR (KBr, ν, cm^{-1}) 3123, 1663, 1623, 1593, 1457, 1340, 1250, 1112, 1021, 858; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.45−7.42 (m, 1H), 7.32 (d, J = 1.6 Hz, 1H), 7.17−7.09 (m, 4H), 6.96−6.90 (m, 2H), 6.70 (d, J = 8.4 Hz, 1H), 6.29−6.26 (m, 1H), 6.02−5.99 (m, 1H), 3.37 (s, 3H), 2.89 (d, J = 14.0 Hz, 1H), 2.21 (d, J = 14.0 Hz, 1H), 1.39 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 185.0, 173.7, 154.2, 153.7, 139.5, 139.2, 137.8, 132.3, 130.9 ($^3J_{CF}$ = 8.2 Hz), 130.7 ($^4J_{CF}$ = 3.3 Hz), 129.6, 128.7 ($^2J_{CF}$ = 21.0 Hz), 122.4, 117.3 ($^1J_{CF}$ = 244.2 Hz), 115.8, 114.6, 57.4, 53.2, 44.1, 30.2, 26.1; HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{25}H_{20}NO_2BrF$ 464.0661; Found 464.0659.

8′-Bromo-3a′,5′-dimethyl-1′-phenyl-3′,3a′-dihydrospiro-[cyclohexa[2,5]diene-1,2′-cyclopenta[c]quinoline]-4,4′(5′H)-dione (**4u**). Orange solid, 46.3 mg, 52% yield; mp 162−164 °C; IR (KBr, ν, cm^{-1}) 2967, 1677, 1667, 1590, 1466, 1341, 1252, 1110, 1019, 855; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.46−7.43 (m, 1H), 7.31−7.28 (m, 4H), 7.07 (d, J = 3.2 Hz, 2H), 6.93−6.90 (m, 2H), 6.69 (d, J = 8.4 Hz, 1H), 6.27 (d, J = 9.6 Hz, 1H), 5.98 (d, J = 10.0 Hz, 1H), 3.37 (s, 3H), 2.90 (d, J = 14.0 Hz, 1H), 2.21 (d, J = 14.0 Hz, 1H), 1.39 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 185.0, 173.8, 154.3, 153.8, 140.4, 139.4, 137.3, 134.4, 132.2, 129.6, 128.9, 128.7, 128.6, 128.5, 122.5, 118.4, 114.6, 57.4, 53.3, 44.2, 30.2, 26.1; HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{25}H_{21}NO_2Br$ 446.0756; Found 446.0752.

7′-chloro-1′-(4-fluorophenyl)-3a′,5′-dimethyl-3′,3a′-dihydrospiro[cyclohexa[2,5]diene-1,2′-cyclopenta[c]quinoline]-4,4′(5′H)-dione (**4v**). Orange solid, 41.1 mg, 49% yield; mp 192−193 °C; IR (KBr, ν, cm^{-1}) 2925, 1674, 1666, 1595, 1458, 1374, 1224, 1156, 1095, 847; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.49−7.43 (m, 2H), 7.33−7.31 (m, 2H), 7.20 (d, J = 8.8 Hz, 1H), 7.10−7.07 (m, 2H), 6.96−6.92 (m, 1H), 6.75 (d, J = 2.4 Hz, 1H), 6.29−6.26 (m, 1H), 6.01−5.98 (m, 1H), 3.35 (s, 3H), 2.90 (d, J = 14.0 Hz, 1H), 2.21 (d, J = 14.0 Hz, 1H), 1.40 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 185.0, 173.9, 154.4, 153.9, 141.5, 138.4, 138.1, 134.3, 131.0 ($^4J_{CF}$ = 3.3 Hz), 130.8 ($^3J_{CF}$ = 8.2 Hz), 128.7, 128.5, 122.7, 117.7 ($^1J_{CF}$ = 283.7 Hz), 116.0 ($^2J_{CF}$ = 21.3 Hz), 57.3, 53.3, 44.1, 30.2, 26.0; HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{25}H_{20}NO_2ClF$ 420.1167; Found 420.1165.

7′-Chloro-3a′,5′-dimethyl-1′-phenyl-3′,3a′-dihydrospiro-[cyclohexa[2,5]diene-1,2′-cyclopenta[c]quinoline]-4,4′(5′H)-dione (**4w**). Orange solid, 45.7 mg, 57% yield; mp 127−128 °C; IR (KBr, ν, cm^{-1}) 3127, 1684, 1665, 1593, 1508, 1401, 1337, 1253, 1104, 835; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.49 (d, J = 8.4 Hz, 2H), 7.46−7.43 (m, 1H), 7.35−7.31 (m, 1H), 7.25 (d, J = 8.0 Hz, 1H), 7.03 (d, J = 8.0 Hz, 2H), 6.94−6.86 (m, 2H), 6.75 (d, J = 7.6 Hz, 1H), 6.28−6.25 (m, 1H), 6.02−5.99 (m, 1H), 3.35 (s, 3H), 2.89 (d, J = 14.0 Hz, 1H), 2.20 (d, J = 14.0 Hz, 1H), 1.38 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 185.0, 174.0, 154.4, 154.0, 141.5, 139.6, 137.6, 134.7, 134.3, 128.9, 128.7(1), 128.7(0), 128.6, 128.4, 122.6, 119.3, 116.3, 57.4, 53.3, 44.2, 30.2, 26.1; HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{25}H_{21}NO_2Cl$ 402.1261; Found 402.1264.

1′,3a′-Diphenyl-5′-tosyl-3′,3a′-dihydrospiro[cyclohexa[2,5]-diene-1,2′-cyclopenta[c]quinoline]-4,4′(5′H)-dione (**4x**). Orange solid, 60.3 mg, 53% yield; mp 216−218 °C; IR (KBr, ν, cm^{-1}) 2946, 1711, 1668, 1540, 1473, 1367, 1221, 1190, 859, 773; ^{1}H NMR (400 MHz, DMSO-d_6; δ, ppm) 7.86 (d, J = 8.0 Hz, 2H), 7.57 (d, J = 8.0 Hz, 2H), 7.51 (d, J = 8.0 Hz, 1H), 7.41−7.37 (m, 3H), 7.28−7.24 (m, 3H), 7.21 (d, J = 7.2 Hz, 1H), 7.17−7.13 (m, 5H), 7.07−7.04 (m, 1H), 6.97 (d, J = 6.8 Hz, 1H), 6.16−6.13 (m, 1H), 5.90−5.82 (m, 2H), 2.87 (d, J = 14.0 Hz, 1H), 2.47 (s, 3H), 2.29 (d, J = 14.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6; δ, ppm) 184.6, 172.0, 152.1, 151.6, 146.2, 144.3, 139.8, 135.9, 134.7, 134.2, 133.2, 130.2, 129.6, 129.1(2), 129.1(0), 128.9(2), 128.9(0), 128.8, 128.3, 127.4(3), 127.4(0), 126.6, 126.4, 125.0, 65.0, 58.1, 46.6, 21.6; HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{36}H_{28}NO_4S$ 570.1739; Found 570.1732.

1′-(4-Chlorophenyl)-3,5-difluoro-3a′,5′-dimethyl-3′,3a′-dihydrospiro[cyclohexa[2,5]diene-1,2′-cyclopenta[c]quinoline]-4,4′(5′H)-dione (**4y**). Orange solid, 43.7 mg, 50% yield; mp 202−204 °C; IR (KBr, ν, cm^{-1}) 2974, 1688, 1666, 1594, 1452, 1398, 1255, 1109, 1012, 879; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 7.33−7.29 (m, 2H), 7.24 (s, 1H), 7.09 (d, J = 8.0 Hz, 1H), 6.97 (d, J = 8.0 Hz, 2H), 6.87−6.79 (m, 3H), 6.29−6.26 (m, 1H), 3.45 (s, 3H), 3.10 (d, J = 14.4 Hz, 1H), 2.39 (d, J = 14.4 Hz, 1H), 1.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 173.7, 171.5 (t, $^3J_{CF}$ = 23.9 Hz), 153.1 (dd, $^2J_{CF}$ = 264.8 Hz), 152.8 (dd, $^1J_{CF}$ = 265.0 Hz), 140.3, 140.0, 135.7, 134.7, 132.1, 130.1, 129.9, 129.8(3), 129.8(0), 129.7(6), 129.4 ($^4J_{CF}$ = 18.1 Hz), 129.2 ($^5J_{CF}$ = 10.7 Hz), 127.9, 123.0, 119.8, 115.4, 53.7, 44.8, 31.0, 30.2, 25.8; HRMS (APCI-TOF) m/z: $[M+H]^+$ Calcd for $C_{25}H_{19}NO_2ClF_2$ 438.1072; Found 438.1079.

3,5-Difluoro-3a′,5′-dimethyl-1′-phenyl-3′,3a′-dihydrospiro-[cyclohexa[2,5]diene-1,2′-cyclopenta[c]quinoline]-4,4′(5′H)-dione (**4z**). Orange solid, 39.5 mg, 49% yield; mp 245−246 °C; IR (KBr, ν, cm^{-1}) 2983, 1690, 1667, 1596, 1458, 1399, 1255, 1103, 1001, 892; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 7.30−7.26 (m, 3H), 7.24 (s, 1H), 7.08 (d, J = 8.4 Hz, 1H), 7.01 (d, J = 7.6 Hz, 2H), 6.83−6.78 (m, 3H), 6.30 (d, J = 10.8 Hz, 1H), 3.45 (s, 3H), 3.11 (d, J = 14.4 Hz, 1H), 2.40 (d, J = 14.4 Hz, 1H), 1.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 173.9, 171.7 (t, $^3J_{CF}$ = 23.8 Hz), 153.0 (dd, $^2J_{CF}$ = 263.9 Hz),

DOI: 10.1021/acs.joc.7b00704
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152.8 (dd, $^{1}J_{CF}$ = 264.6 Hz), 139.9, 139.5, 137.2, 133.6, 130.1 ($^{5}J_{CF}$ = 8.4 Hz), 129.8, 129.4 ($^{4}J_{CF}$ = 10.5 Hz), 128.9, 128.7, 128.1, 128.0, 122.9, 120.1, 115.3, 54.8, 53.7, 44.7, 30.1, 25.9; HRMS (APCI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{25}H_{20}NO_2F_2$ 404.1462; Found 404.1467.

*2-Chloro-1′-(4-chlorophenyl)-3a′,5′-dimethyl-3′,3a′-dihydrospiro[cyclohexa[2,5]diene-1,2′-cyclopenta[c]quinoline]-4,4′(5′H)-dione (**4aa**).* Orange solid, 40.0 mg, 46% yield; mp 246−247 °C; IR (KBr, ν, cm^{-1}) 3123, 1670, 1659, 1594, 1463, 1399, 1231, 1103, 1017, 821; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 7.32−7.29 (m, 1H), 7.25−7.19 (m, 3H), 7.09 (d, *J* = 8.4 Hz, 1H), 7.04 (d, *J* = 7.6 Hz, 2H), 6.86−6.80 (m, 2H), 6.41 (d, *J* = 10.0 Hz, 1H), 6.34 (s, 1H), 3.46 (s, 3H), 3.42 (d, *J* = 14.8 Hz, 1H), 2.26 (d, *J* = 14.4 Hz, 1H), 1.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 184.3, 173.7, 158.4, 152.3, 141.7, 140.0, 135.8, 134.4, 131.9, 130.4, 130.0, 129.8, 128.9, 127.8, 127.3, 122.8, 120.1, 115.3, 62.5, 53.6, 44.4, 30.2, 26.5; HRMS (APCI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{25}H_{20}NO_2Cl_2$ 436.0871; Found 436.0876.

*1′-(4-Chlorophenyl)-3a′,5′-dimethyl-4,4′-dioxo-3′,3a′,4′,5′-tetrahydrospiro[cyclohexa[2,5]diene-1,2′-cyclopenta[c]quinoline]-3-carbonitrile (**4bb**).* Orange solid, 34.1 mg, 40% yield; mp 260−262 °C; IR (KBr, ν, cm^{-1}) 3127, 1675, 1602, 1559, 1464, 1399, 1277, 1105, 1010, 849; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 7.32−7.29 (m, 3H), 7.26−7.23 (m, 2H), 7.10 (d, *J* = 8.0 Hz, 1H), 6.98 (d, *J* = 8.0 Hz, 2H), 6.88−6.85 (m, 2H), 6.48 (d, *J* = 10.0 Hz, 1H), 3.45 (s, 3H), 3.10 (d, *J* = 14.4 Hz, 1H), 2.32 (d, *J* = 14.4 Hz, 1H), 1.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 178.2, 173.5, 163.1, 153.2, 141.5, 140.0, 135.0, 134.9, 131.9, 130.3, 129.4, 129.3, 127.9, 127.6, 123.0, 119.7, 117.2, 115.6, 113.3, 57.8, 54.1, 44.5, 30.2, 26.1; HRMS (APCI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{26}H_{20}N_2O_2Cl$ 427.1213; Found 427.1216.

*3a′,5′-Dimethyl-4,4′-dioxo-1′-phenyl-3′,3a′,4′,5′-tetrahydrospiro[cyclohexa[2,5]diene-1,2′-cyclopenta[c]quinoline]-3-carbonitrile (**4cc**).* Orange solid, 39.2 mg, 50% yield; mp 256−258 °C; IR (KBr, ν, cm^{-1}) 2984, 1718, 1672, 1595, 1474, 1349, 1278, 1107, 1008, 839; ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm) 7.30−7.26 (m, 2H), 7.25−7.20 (m, 3H), 7.10−7.07 (m, 3H), 6.80−6.79 (m, 2H), 6.39 (d, *J* = 9.6 Hz, 1H), 6.31 (s, 1H), 3.47 (s, 3H), 3.43 (d, *J* = 14.8 Hz, 1H), 2.26 (d, *J* = 14.4 Hz, 1H), 1.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm) 178.2, 173.6, 162.8, 153.1, 141.8, 140.0, 135.0, 134.8, 131.9, 130.3, 129.5, 129.4, 128.0, 128.0, 123.1, 119.6, 116.8, 115.5, 113.8, 57.8, 53.9, 44.5, 30.2, 26.1; HRMS (APCI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{26}H_{21}N_2O_2$ 393.1603; Found 393.1605.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00704.

^{1}H and ^{13}C NMR spectra for all pure products (PDF)

X-ray crystallographic data for **4h** (CIF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful for financial support from the NSFC (Nos. 21232004, 21472071, and 21602087), PAPD of Jiangsu Higher Education Institutions, the Outstanding Youth Fund of JSNU (YQ2015003), NSF of Jiangsu Province (BK20151163 and BK20160212), the Qing Lan Project and NSF of Jiangsu Education Committee (15KJB150006), and the Graduate Education Innovation Project of Jiangsu Province (No. KYZZ16_0466).

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DOI: 10.1021/acs.joc.7b00704
J. Org. Chem. 2017, 82, 6621−6628