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Palladium-Catalyzed Construction of Tetracyclic Scaffolds *via* 1,7-Enynes Carbocyclization/Iodophenol Dearomatization Cascade

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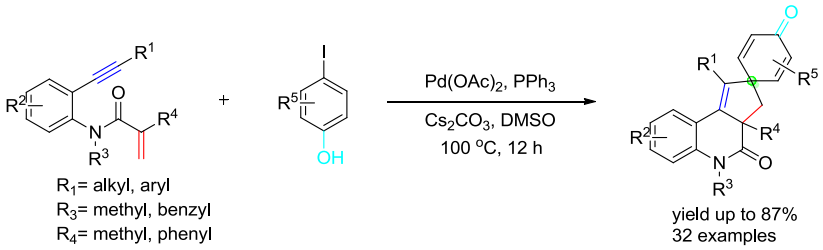
ABSTRACT



An efficient palladium-catalyzed dearomatizing [2+2+1] carbocyclization of 1,7-enynes with iodophenols has been developed. A type of tetracyclic scaffolds was built in this reaction, exhibiting a broad substrate scope with moderate to excellent yields. More importantly, this method provides a potential strategy for the synthesis of tetracyclic skeleton natural products.

INTRODUCTION

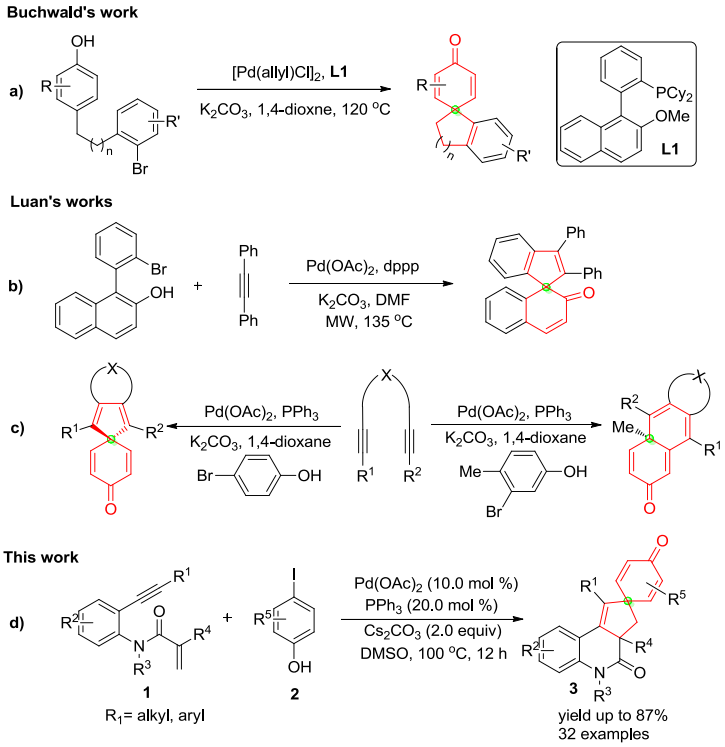
Diverse polycyclic frameworks with spirocyclic units are attractive scaffolds that are present a large number of natural products, bioactive molecules and useful chemical structures.[1] For example, the komarovispirone containing tetracyclic scaffold has trypanocidal activity to against epimastigotes of *T. cruzi.*[1e] As a result of their remarkable pharmacological activities, chemists continues to pay much attention to the ubiquity of many polycyclic frameworks to develop new methods. The traditional strategies of the polycyclic molecules rely on multistep reactions and the synthesis of complex substrates.[2] Recent studies have shown that transition-metal-catalyzed (1, n)-enynes cascade reactions have proven to be a powerful and efficient method for building highly functionalized polycyclic molecules.[3] Specially, palladium-catalyzed transformations with (1, n)-enynes have exhibited fascinating progress in recent years. Including our group[4], various groups[5] have reported great efforts towards characterizing these approaches. In 2017, Li and co-workers[5f] reported a palladium-catalyzed carboannulation of 1,7-enynes with aryl diazonium salts and H_2O to synthesize the polycyclic compounds. The crucial mechanism is that the oxygen atom of carbonyl group is formed by H_2O attack. Because of the highly reactive activity of palladium and the simplicity of (1, n)-enynes, we easily realize designs that could not be achieved through traditional methods. Thus, the development of palladium-catalyzed (1, n)-enynes tandem methods for the construction of polycyclic compounds is still

in great demand.

Dearomatization reactions have proven to be an efficient strategy for the construction of spirocyclic structures from readily available aromatic compounds.[6] Although eminent dearomatization approaches[7] have been realized, including oxidation, cycloaddition, halogenation, allylation and C-H activation, dearomative cascade reactions are still highly desirable due to their significant value in the synthesis of spirocyclic and polycyclic molecules. Phenols and their derivatives are a class of widely distributed chemical starting materials in nature and play an important role in dearomatization transformations. The diversified functionalization of phenol and naphthol derivatives provide a convenient and straightforward way to access the challenging but synthetically valuable dearomative spirocarbocycles,[8] which have already attracted extensive attention with the development of multifariousness of synthetic methods. Very recently, transition-metal-catalyzed tandem reactions as a potent tool has enabled highly efficient construction of dearomatization of indoles, anilines, pyrroles, furans, isoquinolines, especially phenols and so on.[6d, 9] The pioneering dearomatization approaches of phenols which were reported by the groups of Buchwald,[10] You,[11] Hamada,[12] Luan,[13] and others[14] have demonstrated the ability of transition-metal-catalyzed strategies to produce polycyclic frameworks with spirocyclic units. In 2011, Buchwald *et al.*[10] used $[Pd(C_3C_5)Cl]_2$/L1 catalyst system to realize an intramolecular dearomatization

of phenols with excellent yields and chemoselectivity (Scheme 1, 1a). Recently, Luan and co-workers[13a] employed palladium-catalyzed to access a series of spirocyclic compounds through the vinylative dearomatization reaction of *β*-naphthol with alkyne migratory insertion (Scheme 1, 1b). Soon after, Luan *et al*.[13b] further developed a palladium-catalyzed dearomatizing [2+2+x] (x=1 or 2) carbocyclization of tethered diynes with different bromophenols to afford a class of novel tricyclic compounds (Scheme 1, 1c). Although significant advances have been reported towards producing these eminent methods, few examples of the palladium-catalyzed intermolecular dearomatization of enynes with phenols have been reported. Inspired by these studies, we decided to attempt whether palladium can catalyze the cyclization of 1,7-enynes and the dearomatization of phenols to form the corresponding dearomative tetracyclic scaffolds with spirocyclic units. Herein, we describe the successful execution of our design which employed 1,7-enynes and phenols in a one-pot palladium-catalyzed reaction (Scheme 1, 1d).

Scheme 1. Methods toward Diverse Phenols via Palladium-Catalyzed Dearomatization

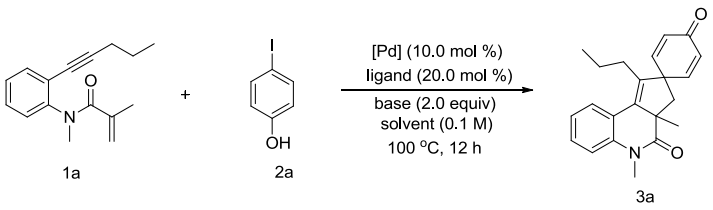


RESULTS AND DISCUSSION

The initial exploration began by employing the classical compound 1,7-enyne **1a** and commercially available 4-iodophenol **2a** as the standard coupling partners to optimize the reaction conditions. The results are summarized in Table 1. Much to our delight, our anticipated reaction was first realized to obtain the desired product **3a** with a 36% yield using $Pd(OAc)_2$ (10.0 mol %), PPh_3 (20.0 mol %), and Cs_2CO_3 (2.0 equiv) in MeCN at 100 ^oC for 12 h (Table 1, entry 1). Subsequently, various solvents were executed (entries 2-5), and the condition was dramatically improved following the use of DMSO as the solvent, providing **3a** in 83% yield. No better results were obtained after further screening on the effect of the base (entries 6-8). Next,

ligands such as XPhos, PCy_3 and P(2-furyl)$_3$ did not give a superior yield (entries 9-11). Other palladium catalysts were investigated along with PPh_3 as the ligand (entries 12-14), but inferior performance was observed in contrast with $Pd(OAc)_2$. The subsequent adjustment of the catalyst/ligand loading ratio and the reaction temperature produced lower yields for the formation of product **3a** (entries 15-16). Finally, we changed **2a** to 4-bromophenol. However, the reaction failed to obtain the product **3a** (entry 17). The optimized reaction conditions were characterized as follows: 10.0 mol % $Pd(OAc)_2$, 20.0 mol % PPh_3 and 2.0 equivalents of Cs_2CO_3 in DMSO at 100 ^oC for 12 h.

Table 1. Optimization of the Reaction Conditions[a]

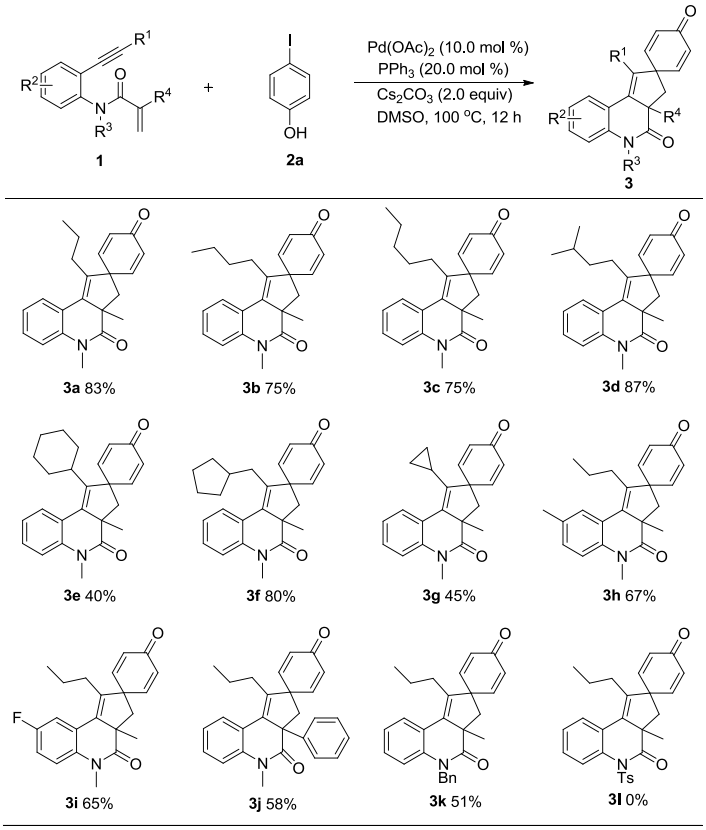


entry	[Pd]	ligand	base	solvent	yield[b] (%)
1	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	MeCN	36
2	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	Toluene	30
3	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	1,4-dioxane	71
4	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	DMF	32
5	**$Pd(OAc)_2$**	**PPh_3**	**Cs_2CO_3**	**DMSO**	**83**
6	$Pd(OAc)_2$	PPh_3	Na_2CO_3	DMSO	42
7	$Pd(OAc)_2$	PPh_3	K_2CO_3	DMSO	70
8	$Pd(OAc)_2$	PPh_3	K_3PO_4	DMSO	57
9	$Pd(OAc)_2$	XPhos	Cs_2CO_3	DMSO	46
10	$Pd(OAc)_2$	PCy_3	Cs_2CO_3	DMSO	70
11	$Pd(OAc)_2$	P(2-furyl)$_3$	Cs_2CO_3	DMSO	66
12	$Pd(MeCN)_2Cl_2$	PPh_3	Cs_2CO_3	DMSO	63
13	$Pd(PPh_3)_2Cl_2$	PPh_3	Cs_2CO_3	DMSO	74
14	$[Pd(allyl)Cl]_2$	PPh_3	Cs_2CO_3	DMSO	67
15[c]	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	DMSO	32
16[d]	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	DMSO	72
17[e]	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	DMSO	nr

[a]Reactions were carried out using **1a** (0.2 mmol), **2a** (0.4 mmol), [Pd] (10.0 mol %), ligand (20.0 mol %), Cs_2CO_3 (2.0 equiv), solvent (0.1 M), 100 °C, 12 h. [b]Isolated yields. [c]$Pd(OAc)_2$ (5 mol %), PPh_3 (10.0 mol %). [d]At 120 °C. [e]**2a** was changed to 4-bromophenol.

Firstly, a series of 1,7-enynes with a terminal alkyne of alkyl groups were tested under the optimized reaction conditions, thus affording the corresponding products (**3a**-**3l**) in moderate to excellent yields (Scheme 2). The terminal alkyne of n-alkyl groups (**1a**-**1c**) could be achieved smoothly with yields of 75-83%. Moreover, various alkyl groups, which possess the cyclohexyl, cyclopropyl, cyclopentyl, and iospentyl substituents on the alkyne termini were employed for the desired cyclization to successfully form the products **3d**-**3g**. Several substituents, such as methyl and fluoro on the aryl of aniline were well-tolerated and provided the tetracyclic compounds with acceptable yields (**3h** and **3i**). In addition, R^4 was changed to phenyl group, corresponding product was obtained in 58% yield (**3j**). Unfortunately, substrate **1l** failed to give the corresponding product 3l. But gratifyingly, nitrogen with benzyl protection carried out the desired product (**3k**) in moderate yield.

Scheme 2. Substrate Scope with Respect to the 1,7-enynes of alkyl group[a]

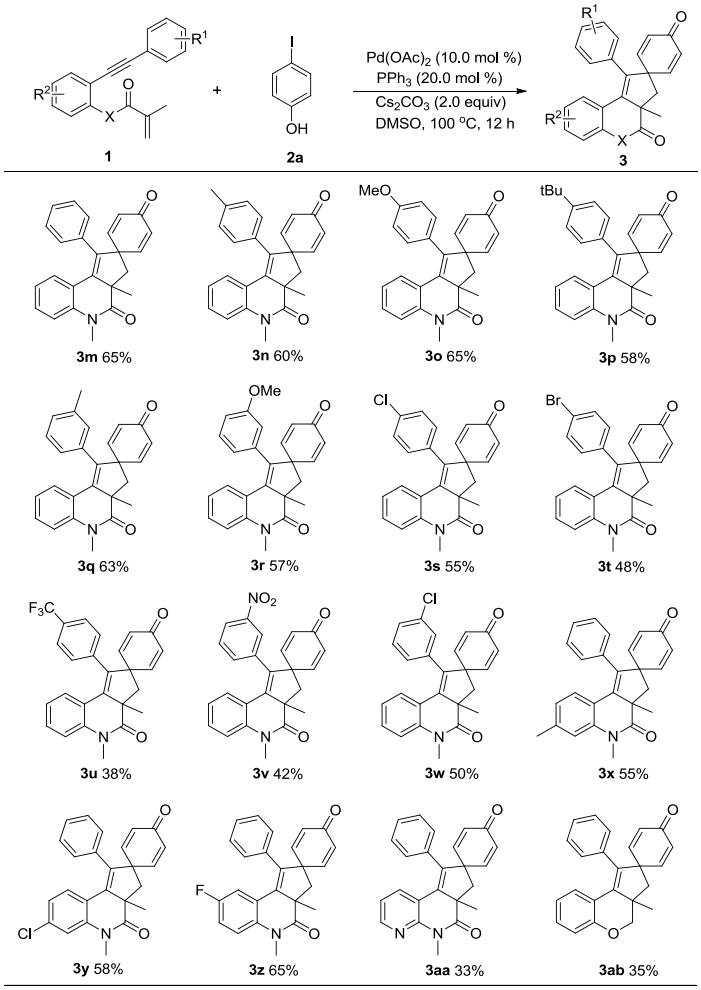


[a]Reaction conditions unless otherwise noted: **1** (0.2 mmol), **2** (0.4 mmol), $Pd(OAc)_2$ (10 mol %), PPh_3 (20 mol %), Cs_2CO_3 (2.0 equiv), DMSO (0.1 M), 100 °C, 12 h. Isolated yields are shown.

To further ascertain the scope of the chosen reaction conditions, a variety of 1,7-enynes with a terminal alkyne of aryl groups were also evaluated (Scheme 3). The fundamental structure of the 1,7-enyne substrate (**1m**) was tested at once, thus affording corresponding product in 65% yield (**3m**). The structure of **3m** was confirmed by X-ray crystal structure analysis (see the Supporting Information). A comparison of the current results with our previous experiments indicated that the alkyl groups on the alkyne termini were more active than the

aryl groups. The presence of electron-donating groups at the *para*- and *meta*-positions, such as methyl, methoxy, *tert*-butyl were tolerated and gave rise to the production of **3n**-**3r** in 57-65% yields. Satisfactorily, various electron-withdrawing groups were also applied at the *para*-, *meta*-positons to afford **3s**-**3w** in 38-55% yields. It is worth mentioning that trifluoromethyl and nitro groups were compatible with this transformation. Furthermore, we tested the electronic effect on the R^2, corresponding reactions proceeded to provide the anticipated products in moderate yield (**3x**-**3z**). Gratifyingly, the novel tetracyclic scaffolds of naphthyridine and chroman were synthesized in 33-35% yields (**3aa** and **3ab**).

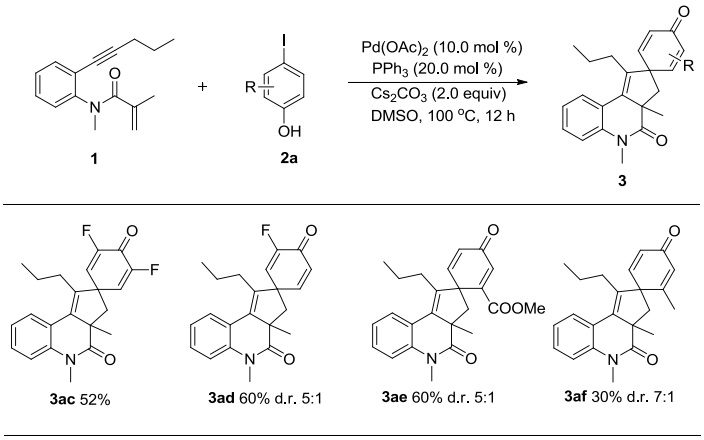
Scheme 3. Substrate Scope with Respect to the 1,7-Enynes of Aryl Groups[a]



[a]Reaction conditions unless otherwise noted: **1** (0.2 mmol), **2** (0.4 mmol), $Pd(OAc)_2$ (10.0 mol %), PPh_3 (20.0 mol %), Cs_2CO_3 (2.0 equiv), DMSO (0.1 M), 100 °C, 12 h. Isolated yields are shown.

Finally, to test the electronic effect of the 4-iodophenols, substrates **2ac**-**2af** were synthesized and subjected to the optimized conditions (Scheme 4). Electron-withdrawing groups were tolerated, such as fluoro and ester, giving **3ac**-**3ae** in 52-60% yields with 5:1-7:1 dr. Electron-donating groups also could be achieved (**3af**), but in a lower yield with 7:1 dr.

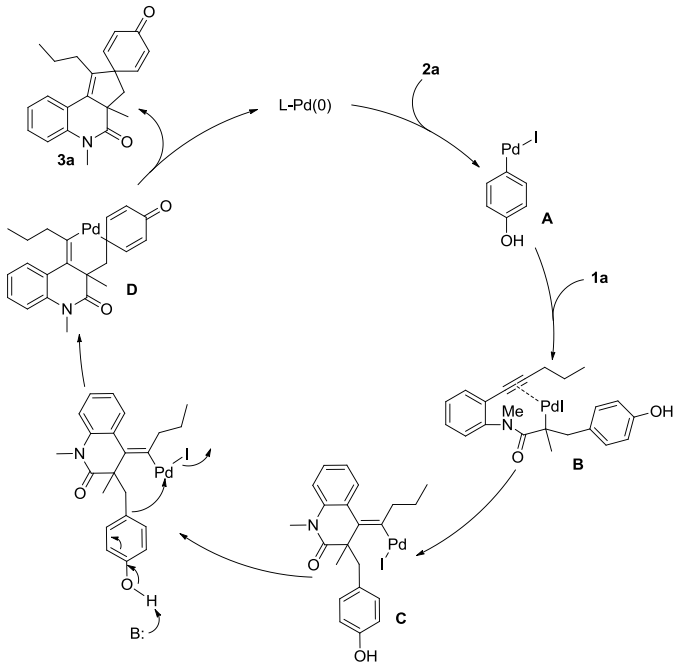
Scheme 4. Substrate Scope with Respect to the Iodophenols[a, b]



[a]Reaction conditions unless otherwise noted: **1** (0.2 mmol), **2** (0.4 mmol), $Pd(OAc)_2$ (10 mol %), PPh_3 (20 mol %), Cs_2CO_3 (2.0 equiv), DMSO (0.1 M), 100 °C, 12 h. Isolated yields are shown. [b]The dr values were determined by ^1H NMR analysis of the crude reaction mixture.

A plausible mechanism for the formation of **3a** is depicted in Scheme 5.[10, 11a, 13b, 15] The catalytic cycle is initiated that the in situ formed Pd(0) undergoes oxidative addition with C-I bond of 4-iodophenol (**2a**). Subsequently, the intermediate **A** is preferred to react with carbon-carbon double bonds in 1,7-enyne (**1a**) to afford the intermediate **B**. The intermediate **B**, which undergoes intramolecular coordination of the alkyne unit to the Pd center, could follow cyclization with alkyne to form vinylpalladium **C**. Under the action of base, the deprotonation reaction is carried out on the hydroxyl group of **C**, the dearomatization occurs at the *ipso*-position and nucleophilic immediately attacks to the Pd (II) center, producing the cyclicpalladium **D**. Finally, the reaction delivered the product **3a** via reductive elimination, meanwhile released the Pd(0) to the next reaction cycle.

Scheme 5. **Proposed Mechanism**



CONCLUSION

In summary, we developed an efficient palladium-catalyzed dearomatizing [2+2+1] carbocyclization of 1,7-enynes with 4-iodophenols to build novel tetracyclic compounds. The 1,7-enynes tolerated both alkyl and aryl groups in the method. Moreover, some heterocycles in tetracyclic scaffolds are also synthesized smoothly, showing a wide application prospects in the synthesis of natural products. More importantly, this method provided a new strategy of transition-metal-catalyzed dearomatization reaction to construct the less-common tetracyclic frameworks.

EXPERIMENTAL SECTION

General Remarks

Column chromatography was carried out on silica gel. ^{1}H NMR spectra were recorded on 400 MHz in $CDCl_3$, ^{13}C NMR spectra were recorded on 100 MHz in $CDCl_3$ and ^{19}F NMR spectra were recorded on 376 MHz in in $CDCl_3$. IR

spectra were recorded on a FT-IR spectrometer and only major peaks are reported in cm^{-1}. All products were further characterized by high resolution mass spectra (HRMS), the HRMS was obtained on a Q-Exactive Hybrid Quadrupole-Orbitrap Mass Sepctrometer. Copies of their ^{1}H NMR, ^{13}C NMR spectra and ^{19}F NMR are provided in the Supporting Information. Room temperature is 23-25°C. MeCN, toluene, 1,4-dioxane were distilled over CaH_2 and DMF, DMSO were reduced pressure distillation over CaH_2.

General Procedure for Synthesis of 1,7-enynes

To a mixture of 2-iodoanilines (12 mmol), $PdCl_2(PPh_3)_2$ (1 mol %) and CuI (2 mol %) in Et_3N (20 ml) were added ethynylbenzene derivatives (1.2 equiv) or alkyl acetylenes (1.2 equiv) under argon atmosphere. The reaction was performed at room temperature overnight. Saturated NH_4Cl solution was added to mixture and extracted with ethyl acetate twice. The combined organic phase was washed with brine and dried over Na_2SO_4. The concentrated residue was purified by column chromatography over silica gel using petroleum ether/ethyl acetate 20:1 to get the anilines.

Next, Methacryloyl chloride (1.2 equiv), was added to a mixture of anilines (1.0 equiv), DMAP (5 mol %), Et_3N (2 equiv) in CH_2Cl_2 (20 ml) at 0 ^{o}C dropwise. After stirring at 0 ^{o}C for 30 min and room temperature overnight, the mixture was quenched with saturated $NaHCO_3$. The mixture was extracted with CH_2Cl_2, washed with brine, and dried over Na_2SO_4. After filtration and concentration, the obtained crude amide was used in next step without purification. NaH

(60 %, in mineral oil, 2.0 equiv) was added to a solution of above crude amide in THF (20 ml) at 0 ^{o}C in portions. After stirring for 30 min at 0 ^{o}C, MeI (3.0 equiv) added dropwise and the reaction mixture was allowed to warm to room temperature and stirred for another 2 h. The reaction was quenched with water and the resulting mixture was extracted with ethyl acetate twice. The combined organic phase was washed with brine and dried over Na_2SO_4. The concentrated residue was purified by column chromatography over silica gel using petroleum ether/ethyl acetate 10:1 to get the 1,7-enynes.[16a]

*N-(2-(phenylethynyl)phenyl)-N-tosylmethacrylamide (**1l**)* was synthesized refer to the reference.[16b]

General Procedure for Synthesis of 3

To a Schlenk tube were added 1,7-enynes **1** (0.20 mmol), phenols **2** (0.4 mmol), $Pd(OAc)_2$ (10 mol %), PPh_3 (20 mol %), Cs_2CO_3 (2 equiv) and DMSO (0.1 M). Then the tube was charged by argon, and was stirred at 100 ^{o}C for 12 h. After the reaction was finished, the mixture was quenched by water and extracted with ethyl acetate twice. The combined organic phase was washed with brine and dried over Na_2SO_4. The concentrated residue was purified by column chromatography over silica gel using petroleum ether/ethyl acetate 4:1 to afford the desired products **3**.

Characterization Data of Products 3a-3af

*3a',5'-dimethyl-1'-propyl-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3a**).* Yellow oil (55.4 mg, 83%). ^{1}H NMR (400

MHz, $CDCl_3$; δ, ppm): 7.42 (dd, *J* =7.6 Hz, 1.3 Hz, 1H), 7.39-7.34 (m, 1H), 7.16-7.12 (m, 1H), 7.13 (d, *J* = 8.2 Hz, 1H), 6.92 (dd, *J* = 9.9 Hz, 3.0 Hz, 1H), 6.69 (dd, *J* = 9.8 Hz, 2.8 Hz, 1H), 6.32 (dd, *J* = 10.0 Hz, 1.9 Hz, 1H), 6.29 (dd, *J* = 9.9 Hz, 1.8 Hz, 1H), 3.41 (s, 3H), 2.90 (d, *J* = 14.5 Hz, 1H), 2.12 (d, *J* = 14.5 Hz, 1H), 2.07-2.02 (m, 2H), 1.51-1.36 (m, 2H), 1.31 (s, 3H), 0.87 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 185.7, 174.7, 153.9, 153.5, 140.4, 139.4, 137.2, 129.1, 128.9, 128.1, 126.8, 122.9, 121.7, 115.1, 57.2, 53.4, 43.5, 30.0, 29.2, 26.1, 23.3, 14.3. IR (neat, cm^{-1}): 2962, 2929, 1665, 1599, 1102, 861, 756. HRMS (ESI): m/z calcd for $C_{22}H_{24}NO_2$ $[M+H]^+$ 334.1802, found 334.1789.

*1'-butyl-3a',5'-dimethyl-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3b**).* Yellow oil (55.5 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.43 (dd, *J* = 7.6 Hz, 1.2 Hz, 1H), 7.39-7.34 (m, 1H), 7.14 (t, *J* = 7.5 Hz, 1H), 7.10 (d, *J* = 8.3, 1H), 6.92 (dd, *J* = 9.9 Hz, 3.0 Hz, 1H), 6.69 (dd, *J* = 9.8 Hz, 2.8 Hz, 1H), 6.33 (dd, *J* = 10.0 Hz, 1.8Hz, 1H), 6.30 (dd, *J* = 9.9 Hz, 1.8 Hz, 1H), 3.41 (s, 3H), 2.90 (d, *J* = 14.5 Hz, 1H), 2.12 (d, *J* = 14.5 Hz, 1H), 2.07 (t, *J* = 7,2 Hz, 2H), 1.45-1.37 (m, 2H), 1.31 (s, 3H), 1.29-1.23 (m, 2H), 0.85 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 185.8, 174.8, 154.1, 153.7, 140.6, 139.4, 137.0, 129.1, 128.9, 128.1, 126.9, 123.0, 121.7, 115.2, 57.2, 53.4, 43.5, 32.1, 30.1, 26.8, 26.1, 23.0, 13.7. IR (neat, cm^{-1}): 2959, 2929, 1665, 1599, 1103, 861, 755. HRMS (ESI): m/z calcd for $C_{23}H_{25}NO_2Na$ $[M+Na]^+$ 370.1778, found 370.1774.

*3a',5'-dimethyl-1'-pentyl-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3c**).* Yellow oil (57.6 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.43 (dd, *J* = 7.6 Hz, 1.2 Hz, 1H), 7.39-7.34 (m, 1H), 7.17-7.12 (m, 1H), 7.10 (d, *J* = 8.2 Hz, 1H), 6.92 (dd, *J* = 10.0 Hz, 2.9 Hz, 1H), 6.69 (dd, *J* = 9.8 Hz, 2.9 Hz, 1H), 6.33 (dd, *J* = 10.0 Hz, 1.8Hz, 1H), 6.30 (dd, *J* = 9.9 Hz, 1.8 Hz, 1H), 3.41 (s, 3H), 2.90 (d, *J* = 14.5 Hz, 1H), 2.12 (d, *J* = 14.5 Hz, 1H), 2.07 (t, *J* = 7,2 Hz, 2H), 1.49-1.36 (m, 2H), 1.31 (s, 3H), 1.28-1.23 (m, 4H), 0.85 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 185.8, 174.7, 154.0, 153.6, 140.5, 139.4, 137.0, 129.0, 128.9, 128.0, 126.8, 122.9, 121.7, 115.1, 57.2, 53.4, 43.5, 32.0, 30.0, 29.5, 27.0, 26.1, 22.1, 13.8. IR (neat, cm^{-1}): 2957, 2929, 1665, 1599, 1103, 861, 754. HRMS (ESI): m/z calcd for $C_{24}H_{27}NO_2Na$ $[M+Na]^+$ 384.1934, found 384.1930.

*1'-isopentyl-3a',5'-dimethyl-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3d**).* Yellow soild (63.0 mg, 87%). mp: 135-137 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.44 (dd, *J* = 7.6 Hz, 1.2 Hz, 1H), 7.39-7.34 (m, 1H), 7.16-7.12 (m, 1H), 7.10 (d, *J* = 8.2 Hz, 1H), 6.92 (dd, *J* = 10.0 Hz, 2.9 Hz, 1H), 6.69 (dd, *J* = 9.8 Hz, 2.9 Hz, 1H), 6.33 (dd, *J* = 10.0 Hz, 1.8Hz, 1H), 6.30 (dd, *J* = 9.9 Hz, 1.8 Hz, 1H), 3.41 (s, 3H), 2.90 (d, *J* = 14.5 Hz, 1H), 2.12 (d, *J* = 14.5 Hz, 1H), 2.08 (t, *J* = 7,2 Hz, 2H), 1.52-1.44 (m, 1H), 1.31 (s, 3H), 1.27-1.18 (m, 2H), 0.85 (d, *J* = 6.6 Hz, 3H), 0.82 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 185.7, 174.7, 154.0, 153.5, 140.6, 139.4, 136.9, 129.1, 128.9, 128.1, 126.8, 122.9, 121.7, 115.1, 57.2, 53.4, 43.5, 38.8,

30.0, 28.6, 26.1, 24.9, 22.2, 22.0. IR (neat, cm^{-1}): 2956, 2937, 1661, 1599, 1106, 859, 755. HRMS (ESI): m/z calcd for $C_{24}H_{28}NO_2$ $[M+H]^+$ 362.2115, found 362.2113.

*1'-cyclohexyl-3a',5'-dimethyl-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3e**).* Yellow soild (30.0 mg, 40%). mp: 168-170 ^oC. ^1H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.39 (d, *J* = 8.4 Hz, 2H), 7.16 (t, *J* = 7.5 Hz, 1H), 7.11 (d, *J* = 8 Hz, 1H), 6.98 (dd, *J* = 9.9 Hz, 2.8 Hz, 1H), 6.87 (dd, *J* = 10.0 Hz, 2.9 Hz, 1H), 6.32 (dd, *J* = 10.0 Hz, 2.9 Hz, 1H), 6.24 (dd, *J* = 10.0 Hz, 2.9 Hz, 1H), 3.41 (s, 3H), 2.91 (d, *J* = 14.5 Hz, 1H), 2.69-2.63 (m, 1H), 2.00 (d, *J* = 14.5 Hz, 1H), 1.76-1.73 (m, 1H), 1.61 (s, 3H), 1.49-1.42 (m, 2H), 1.34-1.28 (m, 2H), 1.21 (s, 3H), 1.1-1.02 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 185.8, 174.7, 155.2, 155.0, 146.0, 139.6, 136.5, 128.8, 127.7, 127.6, 126.8, 122.8, 122.4, 115.2, 56.6, 52.7, 44.4, 39.4, 32.6, 32.5, 30.1, 26.7, 26.4, 25.5, 25.2. IR (neat, cm^{-1}): 2924, 2852, 1662, 1597, 1106, 862, 753. HRMS (ESI): m/z calcd for $C_{25}H_{28}NO_2$ $[M+H]^+$ 374.2115, found 374.2113.

*1'-(cyclopentylmethyl)-3a',5'-dimethyl-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3f**).* Yellow oil (59.8 mg, 80%). ^1H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.55 (dd, *J* = 7.6 Hz, 1.3 Hz, 1H), 7.38-7.34 (m, 1H), 7.15-7.09 (m, 2H), 6.93 (dd, *J* = 9.9 Hz, 2.9 Hz, 1H), 6.76 (dd, 9.8 Hz, 2.9 Hz, 1H), 6.33 (dd, *J* = 10.0 Hz, 1.8Hz, 1H), 6.30 (dd, *J* = 9.9 Hz, 1.8 Hz, 1H), 3.41 (s, 3H), 2.89 (d, *J* = 14.5 Hz, 1H), 2.41-2.36 (m, 1H), 2.12 (d, *J* = 14.5 Hz, 1H), 2.04-1.95 (m, 1H), 1.92-1.85 (m, 1H), 1.60-1.40 (m, 6H), 1.30 (s, 3H),

1.15-1.10 (m, 1H), 0.94-0.88 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 185.8, 174.9, 154.1, 153.9, 140.0, 139.4, 137.4, 128.9, 128.8, 128.1, 127.0, 122.8, 122.0, 115.2, 57.2, 53.4, 43.7, 38.7, 33.0, 32.4, 32.1, 30.0, 25.5, 24.8, 24.7. IR (neat, cm^{-1}): 2952, 2868, 1665, 1599, 1105, 861, 755. HRMS (ESI): m/z calcd for $C_{25}H_{28}NO_2$ $[M+H]^+$ 374.2115, found 374.2110.

*1'-cyclopropyl-3a',5'-dimethyl-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3g**).* Yellow oil (29.9 mg, 45%). ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.70 (dd, *J* = 7.5 Hz, 1.0 Hz, 1H), 7.38-7.34 (m, 1H), 7.14 (t, *J* = 7.5 Hz, 1H), 7.08 (d, *J* = 8.2 Hz, 1H), 6.95 (dd, *J* = 10.4 Hz, 3.1Hz, 1H), 6.85 (dd, *J* = 9.8 Hz, 2.6 Hz, 1H), 6.32-6.28 (m, 2H), 3.40 (s, 3H), 2.86 (d, *J* = 14.4 Hz, 1H), 2.08 (d, *J* = 14.4 Hz, 1H), 1.45-1.40 (m, 1H), 1.29 (s, 3H), 0.80-0.73 (m, 1H), 0.67-0.60 (m, 1H), 0.48-0.43 (m, 1H), 0.39-0.33 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 185.9, 174.8, 155.4, 153.7, 139.7, 139.5, 137.9, 128.9, 128.8, 128.2, 127.9, 122.5, 121.3, 114.9, 57.2, 52.9, 44.1, 30.0, 25.5, 10.0, 9.6, 6.0. IR (neat, cm^{-1}): 3042, 2968, 1664, 1599, 1105, 861, 756. HRMS (ESI): m/z calcd for $C_{22}H_{22}NO_2$ $[M+H]^+$ 332.1645, found 332.1635.

*3a',5',8'-trimethyl-1'-propyl-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3h**).* Yellow oil (46.6 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.21 (s, 1H), 7.16 (d, *J* = 8.3 Hz, 1H), 6.98 (d, *J* = 8.4 Hz, 1H), 6.91 (dd, *J* = 10.0 Hz, 3.0 Hz, 1H), 6.69 (dd, *J* = 9.9 Hz, 2.8 Hz, 1H), 6.35-6.28 (m, 2H), 3.38 (s, 3H), 2.89 (d, *J* = 14.5 Hz, 1H), 2.37 (s, 3H), 2.11 (d, *J* = 14.4 Hz, 1H), 2.08-2.01 (m, 2H), 1.51-1.43 (m, 2H), 1.30 (s, 3H), 0.88 (t, *J*

= 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 185.8, 174.7, 154.0, 153.7, 140.1, 137.4, 137.1, 132.4, 129.4, 129.1, 128.1, 127.5, 121.6, 115.0, 57.2, 53.4, 43.5, 30.0, 29.1, 26.1, 23.3, 20.8, 14.3. IR (neat, cm^{-1}): 2961, 2927, 1666, 1613, 1109, 860, 813. HRMS (ESI): m/z calcd for $C_{23}H_{26}NO_2$ $[M+H]^+$ 348.1958, found 348.1957.

*8'-fluoro-3a',5'-dimethyl-1'-propyl-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3i**).* Yellow oil (45.8 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.12 (dd, *J* = 9.1 Hz, 2.4 Hz, 1H), 7.07-7.05 (m, 2H), 6.89 (dd, *J* = 9.9 Hz, 3.0 Hz, 1H), 6.68 (dd, *J* = 9.8 Hz, 2.9 Hz, 1H), 6.35-6.29 (m , 2H), 3.39 (s, 3H), 2.90 (d, *J* = 14.5 Hz, 1H), 2.12 (d, *J* = 14.5 Hz, 1H), 2.07-2.00 (m, 2H), 1.50-1.42 (m, 2H), 1.31 (s, 3H), 0.89 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, CDCl3; δ, ppm): 185.6, 174.3, 158.4 (d, *J* = 242.0 Hz), 153.4, 153.1, 142.0, 136.3 (d, *J* = 2.2 Hz), 135.8, (d, *J* = 2.9 Hz), 129.2, 128.3, 123.2 (d, *J* = 7.3 Hz), 116.4 (d, *J* = 8.0 Hz) 115.2 (d, *J* = 22.5 Hz), 113.6 (d, *J* = 23.3 Hz), 57.1, 53.2, 43.5, 30.3, 29.0, 26.0, 23.3, 14.3. ^{19}F NMR (376 MHz, $CDCl_3$): δ -119.71. IR (neat, cm^{-1}): 2962, 2928, 1666, 1108, 860, 815, 735. HRMS (ESI): m/z calcd for $C_{22}H_{23}FNO_2$ $[M+H]^+$ 352.1707, found 352.1702.

*5'-methyl-3a'-phenyl-1'-propyl-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3j**).* Yellow soild (45.9 mg, 58%). mp: 204-206 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.57 (dd, *J* = 7.6 Hz, 1.2 Hz, 1H), 7.32-7.25 (m, 3H), 7.23-7.19 (m, 2H), 7.18-7.13 (m, 2H), 6.93 (d, *J* = 8.1 Hz, 1H), 6.74 (dd, *J* = 10.0 Hz, 2.9 Hz, 1H), 6.58 (dd, *J* = 10.0 Hz, 2,9 Hz, 1H),

6.35, (dd, *J* = 10.0 Hz, 2.9Hz, 1H), 6.11 (dd, *J* = 10 Hz, 2.9 Hz, 1H), 3.37 (s, 3H), 3.26 (d, *J* = 14.2 Hz, 1H), 2.36 (d, *J* = 14.2 Hz, 1H), 2.26-2.20 (m, 2H), 1.55-1.42 (m, 2H), 0.95 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 185.8, 172.2, 153.0, 152.8, 144.5, 142.0, 139.4, 134.5, 129.7, 129.0, 128.7, 128.0, 127.4, 126.5, 126.4, 123.2, 122.6, 115.5, 61.0, 57.4, 47.3, 30.4, 29.7, 29.6, 23.4, 14.4. IR (neat, cm^{-1}): 2955, 2926, 1665, 1598, 867, 761, 707. HRMS (ESI): m/z calcd for $C_{27}H_{26}NO_2$ $[M+H]^+$ 396.1958, found 396.1957.

*5'-benzyl-3a'-methyl-1'-propyl-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3k**).* Yellow oil (41.8 mg, 51%). ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.44 (dd, *J* = 7.6 Hz, 1.3 Hz, 1H), 7.34-7.30 (m, 2H), 7.25 (d, *J* = 6.4 Hz, 1H), 7.20 (d, *J* = 7.0 Hz, 3H), 7.11-7.08 (m, 1H), 6.98 (d, *J* = 8.2 Hz, 1H), 6.94 (dd, *J* = 10.0 Hz, 3 Hz, 1H), 6.73 (dd, *J* = 9.8 Hz, 2.8 Hz, 1H), 6.36-6.30 (m, 2H), 5.62 (d, *J* = 16.3 Hz, 1H), 4.75 (d, *J* = 16.3 Hz, 1H), 2.99 (d, *J* = 14.6 Hz, 1H), 2.16 (d, *J* = 14.5 Hz, 1H), 2.11-2.04 (m, 2H), 1.49-1.32 (m, 2H),1.44 (s, 3H), 0.88 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 185.8, 174.9, 154.0, 153.6, 140.6, 138.9, 137.1, 136.9, 129.1, 128.9, 128.2, 127.1, 126.9, 126.0, 123.1, 121.9, 116.0, 57.3, 53.5, 46.7, 43.3, 29.1, 26.1, 23.3, 14.3. IR (neat, cm^{-1}): 2961, 2928, 1665, 1599, 860, 754, 734, 698. HRMS (ESI): m/z calcd for $C_{28}H_{28}NO_2$ $[M+H]^+$ 410.2115, found 410.2112.

*3a',5'-dimethyl-1'-phenyl-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3m**).* Yellow solid (47.8 mg, 65%). mp: 142-144 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.27-7.21 (m, 5H), 7.09-7.05 (m, 3H),

6.87 (dd, *J* = 7.7 Hz, 1.5 Hz, 1H), 6.80 (t, *J* = 7.5 Hz, 1H), 6.66 (dd, *J* = 10.0 Hz, 2,9 Hz, 1H), 6.38 (dd, *J* = 10.0 Hz, 1.9 Hz, 1H), 6.09 (dd, *J* = 10.0 Hz, 1.8 Hz, 1H), 3.45 (s, 3H), 3.01 (d, *J* = 14.3 Hz, 1H), 2.29 (d, *J* = 14.4 Hz, 1H), 1.46 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 185.5, 174.4, 153.4, 153.2, 139.9, 138.7, 134.4, 129.3, 128.9, 128.6, 128.5, 128.2, 128.1, 128.0, 122.7, 120.5, 115.2, 57.3, 53.5, 44.7, 30.0, 25.9. IR (neat, cm^{-1}): 2966, 2926, 1665, 1599, 1105, 861, 754, 731. HRMS (ESI): m/z calcd for $C_{25}H_{22}NO_2$ $[M+H]^+$ 368.1645, found 368.1643.

*3a',5'-dimethyl-1'-(p-tolyl)-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3n**).* Yellow solid (45.8 mg, 60%). mp: 138-140 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.29-7.23 (m, 2H), 7.07 (d, *J* = 8.2 Hz, 1H), 7.01 (d, *J* = 8.0 Hz, 2H), 6.95-6.92 (m, 3H), 6.81 (t, *J* = 7.4 Hz, 1H), 6.65 (dd, *J* = 10.0 Hz, 2.9 Hz, 1H), 6.38 (dd, *J* = 10.0 Hz, 1.8 Hz, 1H), 6.09 (dd, *J* = 10.0 Hz, 1.8 Hz, 1H), 3.45 (s, 3H), 3.00 (d, *J* = 14.5 Hz, 1H), 2.29 (s, 3H), 2.27 (d, *J* = 14.5, 1H), 1.44 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 185.6, 174.5, 153.7, 153.5, 139.8, 138.8, 138.2, 138.0, 131.3, 129.2, 129.1, 128.9, 128.5, 128.0, 127.9, 122.6, 120.7, 115.1, 57.3, 53.4, 44.7, 30.0, 25.8, 21.2. IR (neat, cm^{-1}): 2966, 2926, 1665, 1599, 1105, 862, 746, 731. HRMS (ESI): m/z calcd for $C_{26}H_{24}NO_2$ $[M+H]^+$ 382.1802, found 382.1789.

*1'-(4-methoxyphenyl)-3a',5'-dimethyl-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3o**).* Yellow solid (51.7 mg, 65%). mp: 178-180 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.28-7.24 (m, 2H), 7.08

(d, *J* = 8.2Hz, 1H), 6.99 (d, *J* = 8.6 Hz, 2H), 6.95 (d, *J* = 7.1 Hz, 1H), 6.83 (t, *J* = 7.4 Hz, 1H), 6.73 (d, *J* = 8.6 Hz, 2H), 6.66 (dd, *J* = 10.0 Hz, 2.8 Hz, 1H), 6.39 (dd, *J* = 10.0 Hz, 1.5 Hz, 1H), 6.11 (dd, *J* = 10.0 Hz, 1.5 Hz, 1H), 3.76 (s, 3H), 3.45 (s, 3H), 3.00 (d, *J* = 14.3 Hz, 1H), 2.26 (d, *J* = 14.3 Hz, 1H), 1.43 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 185.6, 174.5, 159.3, 153.9, 153.6, 139.9, 138.3, 137.9, 129.3, 129.2, 128.9, 128.5, 127.9, 126.5, 122.6, 120.8, 115.1, 113.9, 57.2, 55.1, 53.2, 44.8, 30.0, 25.7. IR (neat, cm^{-1}): 2963, 2930, 1664, 1598, 862, 830, 754. HRMS (ESI): m/z calcd for $C_{26}H_{24}NO_3$ $[M+H]^+$ 398.1751, found 398.1737.

*1'-(4-(tert-butyl)phenyl)-3a',5'-dimethyl-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3p**).* Yellow solid (49.2 mg, 58%). mp: 105-107 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.28-7.25 (m, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.07 (d, *J* = 8.2 Hz, 1H), 6.99 (d, *J* = 8.4 Hz, 2H), 6.93 (d, *J* = 6.6 Hz, 1H), 6.82 (t, *J* = 7.5 Hz, 1H), 6.67 (dd, *J* = 10.0 Hz, 2.8 Hz, 1H), 6.39 (dd, *J* = 10.0 Hz, 1.7 Hz, 1H), 6.11 (dd, *J* = 10.0 Hz, 1.8 Hz, 1H), 3.46 (s, 3H), 3.00 (d, *J* = 14.3 Hz, 1H), 2.26 (d, *J* = 14.2 Hz, 1H), 1.44 (s, 3H), 1.27 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 185.8, 174.6, 153.9, 153.7, 151.1, 139.8, 138.7, 138.1, 129.2, 128.9, 128.5, 128.0, 127.6, 125.3, 122.6, 120.8, 115.1, 57.3, 53.4, 44.8, 34.5, 31.1, 30.0, 25.7. IR (neat, cm^{-1}): 2963, 1665, 1599, 1105, 857, 754, 730. HRMS (ESI): m/z calcd for $C_{29}H_{30}NO_2$ $[M+H]^+$ 424.2271, found 424.2259.

3a',5'-dimethyl-1'-(m-tolyl)-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclope

*nta[c]quinoline]-4,4'(5'H)-dione (**3q**).* Yellow solid (48.1 mg, 63%). mp: 192-194 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.28-7.22 (m, 2H), 7.12-7.04 (m, 3H), 6.89 (dd, *J* = 7.6 Hz, 1.3 Hz, 1H), 6.85 (d, *J* = 9.0 Hz, 2H), 6.80 (t, *J* = 7.6 Hz, 1H), 6.66 (dd, *J* = 10.0 Hz, 2.9 Hz, 1H), 6.38 (dd, *J* = 10.0 Hz, 1.8 Hz, 1H), 6.09 (dd, *J* = 10.0 Hz, 1.8 Hz, 1H), 3.45 (s, 3H), 3.00 (d, *J* = 14.3 Hz, 1H), 2.28 (d, *J* = 14.3 Hz, 1H), 2.22 (s, 3H), 1.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 185.5, 174.4, 153.6, 153.3, 139.8, 138.9, 138.4, 138.0, 134.3, 129.2, 128.9, 128.8, 128.6, 128.5, 128.3, 128.0, 125.1, 122.6, 120.6, 115.1, 57.3, 53.4, 44.7, 30.0, 25.9, 21.3. IR (neat, cm^{-1}): 2975, 2931, 1664, 1597, 1104, 867, 769, 758. HRMS (ESI): m/z calcd for $C_{26}H_{24}NO_2$ $[M+H]^+$ 382.1802, found 382.1796.

*1'-(3-methoxyphenyl)-3a',5'-dimethyl-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1 ,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3r**).* Yellow solid (45.4 mg, 57%). mp: 84-86 ^{o}C.^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.29-7.23 (m ,2H), 7.12 (t, *J* = 8.0 Hz, 1H), 7.07 (d, *J* = 8.2 Hz, 1H), 6.94 (dd, *J* = 7.7 Hz, 1.3 Hz, 1H), 6.83 (d, *J* = 7.2 Hz, 1H), 6.78 (dd, *J* = 8.4 Hz, 2.2 Hz, 1H), 6.68-6.60 (m, 3H), 6.38 (dd, *J* = 10.0 Hz, 1.8 Hz, 1H), 6.10 (dd, *J* = 10.0 Hz, 1.8 Hz, 1H), 3.67 (s, 3H), 3.45 (s, 3H), 3.00 (d, *J* = 14.3 Hz, 1H), 2.28 (d, *J* = 14.3 Hz, 1H), 1.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 185.5, 174.4, 159.4, 153.4, 153.3, 139.8, 138.8, 138.4, 135.7, 129.6, 129.4, 128.9, 128.6, 128.1, 122.7, 120.5, 120.4, 115.1, 113.6, 57.2, 55.1, 53.4, 44.7, 30.0, 25.9. IR (neat, cm^{-1}): 2975, 2930, 1664, 1597, 1105, 867, 769, 758. HRMS (ESI): m/z calcd for $C_{26}H_{24}NO_3$ $[M+H]^+$ 398.1751, found 398.1736.

*1'-(4-chlorophenyl)-3a',5'-dimethyl-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3s**).* Yellow solid (44.2 mg, 55%). mp: 204-206 ^{o}C.^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.32-7.27 (m, 1H), 7.23 (dd, *J* = 10.0 Hz, 2.9 Hz, 1H), 7.19 (d, *J* = 8.4 Hz, 2H), 7.09 (d, *J* = 8.2 Hz, 1H), 7.01 (d, *J* = 8.4 Hz, 2H), 6.89-6.82 (m, 2H), 6.63 (dd, *J* = 10.0 Hz, 2.9 Hz, 1H), 6.39 (dd, *J* = 10.0 Hz, 1.7 Hz, 1H), 6.11 (dd, *J* = 10.0 Hz, 1.8 Hz, 1H), 3.45 (s, 3H), 3.01 (d, *J* = 14.4 Hz, 1H), 2.29 (d, *J* = 14.4 Hz, 1H), 1.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 185.3, 174.2, 153.1, 153.0, 139.9, 139.5, 137.1, 134.1, 132.9, 129.6, 129.4, 129.1, 128.8, 128.7, 127.9, 122.8, 120.2, 115.3, 57.1, 53.5, 44.7, 30.0, 25.8. IR (neat, cm^{-1}): 2966, 2944, 1662, 1600, 1105, 861, 828, 752. HRMS (ESI): m/z calcd for $C_{25}H_{21}ClNO_2$ $[M+H]^+$ 402.1255, found 402.1245.

*1'-(4-bromophenyl)-3a',5'-dimethyl-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3t**).* Yellow solid (44.9 mg, 48%). mp: 101-103 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.34 (d, *J* = 8.4 Hz, 2H), 7.30-7.27 (m, 1H), 7.22 (dd, *J* = 10.0 Hz, 2.9 Hz, 1H), 7.09 (d, *J* = 8.2 Hz, 1H), 6.95 (d, *J* = 8.4 Hz, 2H), 6.89-6.84 (m, 2H), 6.62 (dd, *J* = 10.0 Hz, 2.8 Hz, 1H), 6.39 (dd, *J* = 10.0 Hz, 1.7 Hz, 1H), 6.12 (dd, *J* = 10.0 Hz, 1.8 Hz, 1H), 3.45 (s, 3H), 3.00 (d, *J* = 14.4 Hz, 1H), 2.29 (d, *J* = 14.3 Hz, 1H), 1.45 (s ,3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 185.3, 174.2, 153.1, 153.0, 139.9, 139.5, 137.2, 133.3, 131.8, 129.7, 129.6, 129.2, 128.8, 127.9, 122.8, 122.4, 120.2, 115.3, 57.0, 53.5, 44.7, 30.1, 25.8. IR (neat, cm^{-1}): 2962, 2926, 1664, 1599, 1104,

857, 821, 753. HRMS (ESI): m/z calcd for $C_{25}H_{20}BrNO_2Na$ $[M+Na]^+$ 468.0570, found 468.0553.

*3a',5'-dimethyl-1'-(4-(trifluoromethyl)phenyl)-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3u**).* Yellow solid (33.1 mg, 38%). mp: 81-83 ^oC. ^1H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.49 (d, *J* = 8.2 Hz, 2H), 7.33-7.29 (m, 1H), 7.26-7.24 (m, 1H), 7.21 (d, *J* = 8.1 Hz, 2H), 7.11 (d, *J* = 8.2 Hz, 1H), 6.86-6.80 (m, 2H), 6.64 (dd, *J* = 10.0 Hz, 2.9 Hz, 1H), 6.43 (dd, *J* = 10.0 Hz, 1.8 Hz, 1H), 6.13 (dd, *J* = 10.0 Hz, 1.8 Hz, 1H), 3.46 (s, 3H), 3.05 (d, *J* = 14.4 Hz, 1H), 2.34 (d, *J* = 14.4 Hz, 1H), 1.47 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 185.2, 174.2, 152.8 (d, *J* = 1.45 Hz), 140.5, 140.0, 138.3, 136.9, 130.2 (q, *J* = 32.1 Hz), 130.0, 129.3, 128.9, 128.5, 127.9, 126.5 (q, J = 269.6 Hz), 125.5 (q, J = 3.6 Hz), 119.9, 115.4, 57.1, 53.7, 44.8, 30.1, 25.8. ^{19}F NMR (376 MHz, $CDCl_3$): δ -62.7. IR (neat, cm^{-1}): 2976, 2929, 1666, 1599, 1106, 857, 754. HRMS (ESI): m/z calcd for $C_{26}H_{21}F_3NO_2$ $[M+H]^+$ 436.1519, found 436.1502.

*3a',5'-dimethyl-1'-(3-nitrophenyl)-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3v**).* Yellow solid (34.7 mg, 42%). mp: 198-200 ^oC. ^1H NMR (400 MHz, $CDCl_3$; δ, ppm): 8.14-8.11 (m, 1H), 7.95 (t, *J* = 1.6 Hz, 1H), 7.47-7.41 (m, 2H), 7.34-7.29 (m, 1H), 7.28-7.24 (m, 1H), 7.12 (d, *J* = 8.2 Hz, 1H), 6.83-6.79 (m, 1H), 6.76 (q, *J* = 7.7 Hz, 1.6 Hz, 1H), 6.65 (dd, *J* = 10.0 Hz, 3.0 Hz, 1H), 6.43 (dd, *J* = 10.0 Hz, 1.8 Hz, 1H), 6.11 (dd, *J* = 10.0 Hz, 1.9 Hz, 1H), 3.47 (s, 3H), 3.05 (d, *J* = 14.5 Hz, 1H), 2.35 (d, *J* = 14.4 Hz, 1H),

1.49 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 184.9, 173.9, 152.4, 152.3 148.2, 141.4, 140.0, 136.2, 135.5, 134.2, 130.2, 129.7, 129.4, 129.1, 127.5, 123.4, 123.1, 122.9, 119.5, 115.6, 57.0, 53.8, 44.6, 30.1, 26.0. IR (neat, cm^{-1}): 2979, 2934, 1665, 1597, 1105, 869, 782, 760. HRMS (ESI): m/z calcd for $C_{25}H_{21}N_2O_4$ $[M+H]^+$ 413.1496, found 413.1485.

*1'-(3-chlorophenyl)-3a',5'-dimethyl-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3w**).* Yellow solid (40.2 mg, 50%). mp: 200-202 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.32-7.27 (m, 1H), 7.24-7.14 (m, 3H), 7.08 (d, *J* = 8.3 Hz, 1H), 7.05 (s, 1H), 6.95 (d, *J* = 7.6 Hz, 1H), 6.87-6.81 (m, 2H), 6.64 (dd, *J* = 10.0 Hz, 2.8 Hz, 1H), 6.39 (dd, *J* = 10.0 Hz, 1.6 Hz, 1H), 6.11 (dd, *J* = 10.0 Hz, 1.6 Hz, 1H), 3.45 (s, 3H), 3.01 (d, *J* = 14.4 Hz, 1H), 2.29 (d, *J* = 14.4Hz, 1H), 1.46 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 185.2, 174.2, 152.9, 152.7, 140.0, 139.9, 136.9, 134.3, 129.8, 129.7, 129.2, 128.9, 128.4, 128.2, 127.9, 126.3, 122.8, 120.0, 115.3, 57.1, 53.6, 44.7, 30.1, 25.9. IR (neat, cm^{-1}): 2976, 2931, 1663, 1596, 1105, 863, 760, 685. HRMS (ESI): m/z calcd for $C_{25}H_{21}ClNO_2$ $[M+H]^+$ 402.1255, found 402.1253.

*3a',5',7'-trimethyl-1'-phenyl-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3x**).* Yellow solid (42.0 mg, 55%). mp: 166-168 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.27-7.18 (m, 4H), 7.05 (dd, *J* = 7.6 Hz, 1.4 Hz, 2H), 6.88 (s, 1H), 6.75 (d, *J* = 7.8 Hz, 1H), 6.67-6.60 (m, 2H), 6.37 (dd, *J* = 10.0 Hz, 1.8 Hz, 1H), 6.08 (dd, *J* = 10.0 Hz, 1.8 Hz, 1H), 3.44 (s, 3H), 2.99 (d, *J* = 14.3 Hz, 1H), 2.34 (s, 3H), 2.27 (d, *J* = 14.3 Hz, 1H), 1.45 (s,

3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 185.5, 174.6, 153.6, 153.4, 139.9, 139.6, 138.8, 137.6, 134.6, 128.9, 128.5, 128.4, 128.1, 128.0, 127.8, 123.5, 117.8, 115.9, 57.2, 53.5, 44.7, 30.0, 25.9, 21.8. IR (neat, cm^{-1}): 2996, 2927, 1662, 1607, 1104, 860, 818, 695. HRMS (ESI): m/z calcd for $C_{26}H_{24}NO_2$ $[M+H]^+$ 382.1802, found 382.1793.

*7'-chloro-3a',5'-dimethyl-1'-phenyl-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3y**).* Yellow solid (46.6 mg, 58%). mp: 180-182 ^{o}C.^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.27-7.20 (m, 4H), 7.07 (s, 1H), 7.03 (dd, *J* = 7.6 Hz, 1.2 Hz, 2H), 6.68 (s, 2H), 6.64 (dd, *J* = 10.0 Hz, 2.9 Hz, 1H), 6.39 (dd, *J* =10.0 Hz, 1.8 Hz, 1H), 6.09 (dd, *J* = 10.0 Hz, 1.8 Hz, 1H), 3.43 (s, 3H), 2.99 (d, *J* = 14.3 Hz, 1H), 2.29 (d, *J* = 14.3 Hz, 1H), 1.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 185.4, 174.3, 153.1, 152.8, 141.0, 139.4, 137.5, 135.0, 134.0, 129.0, 128.9, 128.7, 128.6, 128.3, 122.7, 118.9, 115.5, 57.2, 53.3, 44.6, 30.1, 25.9. IR (neat, cm^{-1}): 2966, 2926, 1664, 1593, 1094, 863, 850, 729, 700. HRMS (ESI): m/z calcd for $C_{25}H_{21}ClNO_2$ $[M+H]^+$ 402.1255, found 402.1240.

*8'-fluoro-3a',5'-dimethyl-1'-phenyl-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3z**).* Yellow solid (23.9 mg, 31%). mp: 165-167 ^{o}C.^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.28-7.20 (m, 4H), 7.06-7.01 (m, 3H), 6.99-6.94 (m, 1H), 6.65 (dd, *J* = 10.0 Hz, 3.0 Hz, 1H), 6.54 (dd, *J* = 10.0 Hz, 2.8 Hz, 1H), 6.39 (dd, *J* = 10.0 Hz, 1.8 Hz, 1H), 6.09 (dd, *J* = 10.0 Hz, 1.8 Hz, 1H), 3.44 (s, 3H), 3.01 (d, *J* = 14.4 Hz, 1H), 2.30 (d, *J* = 14.3 Hz, 1H),

1.46 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 185.3, 173.9, 158.0 (d, *J* = 241.6 Hz), 153.0, 152.7, 140.3, 137.7 (d, *J* = 1.8 Hz), 136.2 (d, *J* = 2.6 Hz), 133.7, 129.0, 128.8, 128.6, 128.5, 127.9, 122.0 (d, *J* = 8.3 Hz), 116.4 (d, *J* = 8.3 Hz), 115.9 (d, *J* = 22.8 Hz), 114.4 (d, *J* = 23.8 Hz), 57.2, 53.2, 44.6, 30.3, 25.8. ^{19}F NMR (376 MHz, $CDCl_3$): δ -119.8. IR (neat, cm^{-1}): 2968, 2927, 1690, 1664, 1109, 868, 813, 699. HRMS (ESI): m/z calcd for $C_{25}H_{21}FNO_2$ $[M+H]^+$ 386.1551, found 386.1537.

*5',6a'-dimethyl-9'-phenyl-6a',7'-dihydrospiro[cyclohexa[2,5]diene-1,8'-cyclopenta[c][1,8]naphthyridine]-4,6'(5'H)-dione (**3aa**).* Yellow solid (24.4 mg, 33%). mp: 178-180 ^{o}C.^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 8.26 (dd, *J* = 4.9 Hz, 1H), 7.29-7.21 (m, 4H), 7.11 (dd, *J* = 7.6 Hz, 1.8 Hz, 1H), 7.03 (m, 2H), 6.73 (dd, *J* = 7.6 Hz, 4.9 Hz, 1H), 6.65 (dd, *J* = 10.0 Hz, 2.9 Hz, 1H), 6.39 (dd, *J* = 10.0 Hz, 1.8 Hz, 1H), 6.10 (dd, *J* = 10.0 Hz, 1.8 Hz, 1H), 3.56 (s, 3H), 3.03 (d, *J* = 14.4 Hz, 1H), 2.33 (d, *J* = 14.4 Hz, 1H), 1.50 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 185.4, 174.9, 152.9, 152.5, 151.4, 147.8, 141.1, 136.7, 135.5, 133.7, 129.2, 128.9, 128.7, 128.5, 127.9, 118.0, 115.7, 57.2, 53.7, 44.6, 28.9, 26.6. IR (neat, cm^{-1}): 2970, 2948, 1672, 1663, 1106, 864, 776, 702. HRMS (ESI): m/z calcd for $C_{24}H_{21}N_2O_2$ $[M+H]^+$ 369.1598, found 369.1584.

*3a'-methyl-1'-phenyl-3a',4'-dihydro-3'H-spiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]chromen]-4-one (**3ab**).* Yellow solid (25.4 mg, 35%). mp: 198-200 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.33 (dd, *J* = 10.0 Hz, 2.9 Hz, 1H), 7.27-7.25 (m, 3H), 7.12-7.09 (m, 3H), 6.89 (d, *J* = 8.2 Hz, 1H), 6.74 (dd, *J* = 7.9 Hz, 1.3

Hz, 1H), 6.65-6.56 (m, 2H), 6.33 (dd, *J* = 10.0 Hz, 1.7 Hz, 1H), 10.0 Hz, 1.7 Hz, 1H), 4.29 (d, *J* = 10.2 Hz, 1H), 4.02 (d, *J* = 10.2 Hz, 1H), 2.13 (s, 2H), 1.43 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 185.7, 154.2, 153.6, 153.4, 139.2, 135.3, 134.0, 129.9, 129.0, 128.6, 128.2, 128.1, 127.9, 120.3, 117.9, 116.9, 77.2, 57.6, 45.4, 44.3, 23.2. IR (neat, cm^{-1}): 3036, 2964, 2925, 1660, 1617, 1242, 867, 751, 696. HRMS (ESI): m/z calcd for $C_{24}H_{20}O_2Na$ $[M+Na]^+$ 363.1356, found 363.1340.

*3,5-difluoro-3a',5'-dimethyl-1'-propyl-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1, 2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3ac**).* Yellow oil (38.5 mg, 52%). ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.42-7.37 (m, 2H), 7.18-7.14 (m, 1H), 7.11 (d, *J* = 8.2 Hz, 1H), 6.51 (dd, *J* = 11.5 Hz, 2.5 Hz, 1H), 6.33 (dd, *J* = 11.6 Hz, 2.4 Hz, 1H), 3.41 (s, 3H), 3.01 (d, *J* = 14.6 Hz, 1H), 2.22 (d, *J* = 14.6 Hz, 1H), 2.11-1.98 (m, 2H), 1.45-1.34 (m, 2H), 1.31 (s, 3H), 0.91 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 174.2, 171.8 (t, *J* = 24.1 Hz), 154.1 (dd, *J* = 84.7 Hz, 8.0 Hz), 151.5 (dd, *J* = 84.7 Hz, 8.1 Hz), 139.5, 138.7, 137.9, 130.1 (dd, *J* = 10.9 Hz, 2.1 Hz), 129.9 (dd, *J* = 11.0 Hz, 1.6 Hz), 129.3, 126.9, 123.2, 121.3, 115.3, 54.6 (t, *J* = 5.5 Hz), 53.5, 43.7, 30.1, 28.9, 25.8, 23.6, 14.3. ^{19}F NMR (376 MHz, $CDCl_3$): δ – 129.26 (d, *J* =15.1 Hz) -130.02 (d, *J* = 15.0 Hz). IR (neat, cm^{-1}): 2964, 2932, 1687, 1669, 1599, 1002, 756. HRMS (ESI): m/z calcd for $C_{22}H_{22}F_2NO_2$ $[M+H]^+$ 370.1613, found 370.1613.

*3-fluoro-3a',5'-dimethyl-1'-propyl-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3ad**).* Yellow oil (44.9 mg, 60%). ^{1}H

NMR (400 MHz, $CDCl_3$; δ, ppm): 7.43-7.36 (m, 2H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.11 (d, *J* = 8.2 Hz, 1H), 6.92 (dd, *J* = 9.8 Hz, 2.3 Hz, 1H), 6.34-6.30 (m, 1H), 6.26 (dd, *J* = 12.8 Hz, 2.5 Hz, 1H), 3.41 (s, 3H), 2.94 (d, *J* = 14.6 Hz, 1H), 2.20 (d, *J* = 14.5 Hz, 1H), 2.10-2.03 (m, 2H), 1.47-1.37 (m, 2H), 1.31 (s, 3H), 0.89 (t, *J* = 7.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 178.4 (d, *J* = 21.1 Hz), 174.5, 153.9 (d, *J* = 263.6 Hz), 154.6 (d, *J* = 2.2 Hz), 139.6, 139.5, 137.6, 129.1, 128.9 (d, *J* = 11.1 Hz), 127.4 (d, *J* = 4.5 Hz), 126.8, 123.0, 121.5, 115.2, 58.1 (d, *J* = 5.6 Hz), 53.4, 43.7, 30.0, 29.1, 25.9, 23.3,14.3. ^{19}F NMR (376 MHz, CDCl3): δ –129.50, -130.14. IR (neat, cm^{-1}): 2962, 2929, 1678, 1600, 1102, 756. HRMS (ESI): m/z calcd for $C_{22}H_{22}FNO_2Na$ $[M+Na]^+$ 374.1527, found 374.1522.

*Methyl-3a',5'-dimethyl-4,4'-dioxo-1'-propyl-3',3a',4',5'-tetrahydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-2-carboxylate (**3ae**).* Yellow oil (47.0 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$; δ, ppm): 7.58 (d, *J* = 3.0 Hz, 1H), 7.43-7.36 (m, 2H), 7.17-7.10 (m, 2H), 6.67 (dd, *J* = 9.9 Hz, 2,9 Hz, 1H), 6.37 (d, *J* = 10.0 Hz, 1H), 3.88 (s, 3H), 3.41 (s, 3H), 2.94 (d, *J* = 14.7 Hz, 1H), 2.20 (d, *J* = 14.6 Hz, 1H), 2.06-2.02 (m, 2H), 1.47-1.38 (m, 2H), 1.34 (s, 3H), 0.87 (t, *J* = 7.3Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 181.1, 174.4, 164.9, 158.7, 151.7, 139.4, 139.3, 138.3, 130.4, 129.7, 129.2, 126.8, 123.0, 121.4, 115.1, 57.1, 53.6, 52.4, 43.4, 30.0, 29.1, 26.0, 23.2, 14.3. IR (neat, cm^{-1}): 2959, 2927, 1736, 1666, 1602, 1103, 758. HRMS (ESI): m/z calcd for $C_{24}H_{26}NO_4$ $[M+H]^+$ 392.1856, found 392.1856.

*2,3a',5'-trimethyl-1'-propyl-3',3a'-dihydrospiro[cyclohexa[2,5]diene-1,2'-cyclopenta[c]quinoline]-4,4'(5'H)-dione (**3af**).* Yellow oil (20.9 mg, 30%). ^{1}H NMR (400 MHz, CDCl3; δ, ppm): 7.39-7.35 (m, 2H), 7.16-7.09 (m, 2H), 6.59 (d, *J* = 9.8 Hz, 1H), 6.27 (s, 1H), 6.20 (dd, *J* = 9.8 Hz, 1.8 Hz, 1H), 3.42 (s, 3H), 3.06 (d, *J* = 15.2 Hz, 1H), 2.03 (d, *J* = 1Hz, 3H), 2.02 (d, *J* = 15.1 Hz, 1H), 1.95-1.85 (m, 2H), 1.40-1.32 (m, 2H), 1.28 (s, 3H), 0.82 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$; δ, ppm): 186.6, 174.5, 161.0, 154.3, 141.2, 1391.2, 138.0, 129.0, 128.8, 126.9, 126.7, 122.9, 122.6, 115.1, 60.6, 53.5, 41.1, 30.3, 28.9, 25.6, 23.2, 21.1, 14.5. IR (neat, cm^{-1}): 2965, 2928, 1658, 1600, 1104, 758. HRMS (ESI): m/z calcd for $C_{23}H_{26}NO_2$ $[M+H]^+$ 348.1958, found 348.1957.

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Supporting Information

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Crystallographic file of **3m** (CIF)

Copies of ^{1}H NMR, ^{13}C NMR spectra, ^{19}F NMR and GC-MS spectra. (PDF)

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Notes

The authors declare no competing financial interest.

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