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One-Pot Consecutive Sulfonamidation/*ipso*-Cyclization Strategy for the Construction of Azaspirocyclohexadienones

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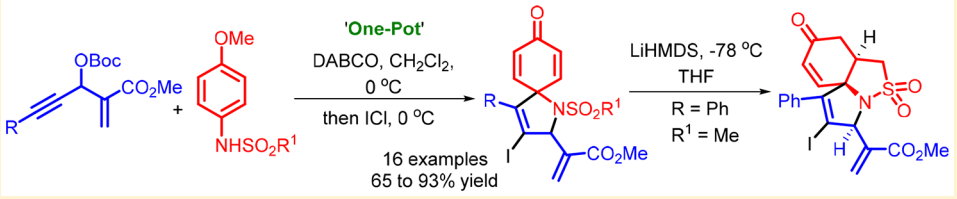
Supporting Information



ABSTRACT: Harnessing of Morita–Baylis–Hillman (MBH) carbonates of acetylenic aldehydes as handy synthons has allowed a facile synthesis of azaspirocyclohexadienones by sequential DABCO-promoted sulfonamidation/ICl-mediated *ipso*-iodocyclization reactions. A variety of MBH-carbonates having aryl or heteroaryl groups on the alkyne functionality fruitfully participated in the one-pot *ipso*-annulation reaction to provide the corresponding 3-iodo spirocyclohexadienones. The sulphonamide functionality was further utilized to construct the tricyclic fused-sultam framework.

INTRODUCTION

During the past decade, synthesis of functionalized spirocylcohexadienones through *ipso*-cyclization has received considerable attention[1] due to their remarkable biological activities (Figure 1) and potential utility for forming charge-transfer complexes.[2]

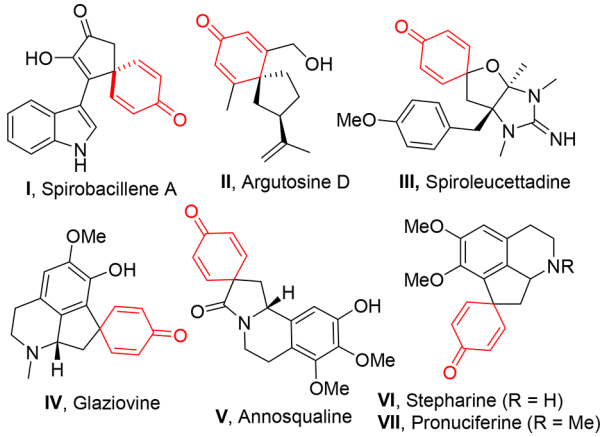
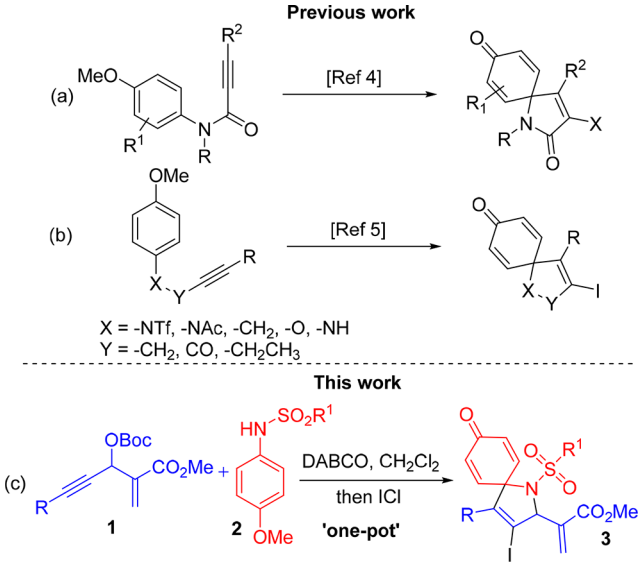


Figure 1. Prevalence of spirocyclohexadienone in bioactive natural products.

In addition, these cyclohexadienones serve as key intermediates to access polycyclic molecular frameworks as well as natural products via synthetic manipulations.[3] Indeed, several *ipso*-annulation approaches to spirocylcohexadienones have been developed. Majority of them involves the halogen or their derivative induced electrophilic cyclization of *N*-arylpropiolamide precursors (Scheme 1a),[4] besides few nonamide substrates (Scheme 1b)[5] toward the synthesis of azaspirocylcohexadienones. All these effective methods require preconstruction of the desired alkynyl amide or amine. Considering the importance of azaspirocylcohexadienones, the development of new strategies is required for their one-pot synthesis.

Scheme 1. *ipso*-Cyclization to Azaspirocyclohexadienones



Our research group has investigated the one-pot reactions using 1-aryl propargylic alcohols[6] and Morita–Baylis–Hillman

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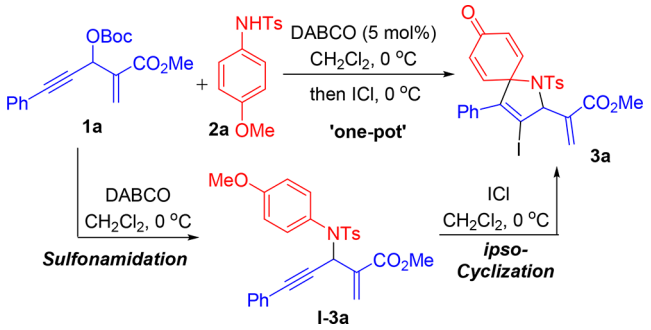
Table 1. Optimization of Reaction Conditions[a]



entry	(sulfonamidation) catalyst (5 mol%), solvent, temp, time	(*ipso*-cyclization) reagent (1 equiv), solvent, temp, time	product	yield (%)
1	DABCO, CH_3CN, 0 °C, 30 min		**I-3a**	45
2	DABCO, CH_2CI_2, 0 °C, 30 min		**I-3a**	81
3[b]	CH_2CI_2, 0 °C 30 min		**I-3a**	
4		$I_2/NaHC0_3$, toluene, −78 °C, 6 h	**3a**	23
5		$I_2/NaHC0_3$, CH_2CI_2, −78 °C, 6 h	**3a**	31
6		$I_2/NaHC0_3$, CH_2CI_2, 0 °C, 6 h	**3a**	30
7		ICl, toluene, −78 °C, 1 h	**3a**	58
8		ICl, CH_2CI_2, −78 °C, 1 h	**3a**	68
9		ICl, CH_2CI_2, 0 °C, 30 min	**3a**	84
10[c]	**DABCO, CH_2CI_2, 0 °C, 30 min**	**ICl, CH_2CI_2, 0 °C, 30 min**	**3a**	**81**

[a]MBH-carbonate (1 equiv) and *N*-(4-methoxyphenyl)-tolylsulfonamide (1.1 equiv). [b]In absence of catalyst, no reaction occurred. [c]One-pot reaction.

adducts of acetylenic aldehydes[7] toward the synthesis of various heterocycles, carbocycles, aromatic and polyaromatic hydrocarbons. The use of these substrates has been proven to be highly convenient for the formation of desired intermediate followed by its annulation in a single reaction vessel, which minimizes the solvent usage and chemical waste generated. Encouraged by the realization that MBH-adduct of acetylenic aldehyde has the potential to construct the spirocyclohexadienones if identified suitable reaction conditions, we envisaged a new one-pot approach to azaspirocyclohexadienones through sequential sulfonamidation/*ipso*-cyclization reaction strategy (Scheme 1c).

RESULTS AND DISCUSSION

This new strategy was planned in such a way that, the *N*-aryl propargylamine (precursor for *ipso*-cyclization) would be generated through the sulfonamidation reaction of MBH-carbonate **1** of acetylenic aldehyde with *N*-arylsulfonamide **2** and subjected to electrophilic *ipso*-halocyclization in one-pot to obtain the corresponding azaspirocylcohexadienones **3**. To the best of our knowledge, there are no earlier reports for the sulfonamidation of MBH-carbonate **1** with *N*-arylsulfonamide **2**, while very limited methods available with primary sulphonamides or *N*-alkylsulfonamides.[8] Furthermore, examples of the *ipso*-cyclization of *N*-aryl propargylsulfonamides are rare.[5b] Herein, we report the first example of one-pot sulfonamidation/*ipso*-cyclization strategy to azaspirocyclohexadienones.

As a starting point, we investigated the reaction of MBH-carbonate **1a** and *N*-(4-methoxyphenyl)-tolylsulfonamide **2a** to find the suitable reaction condition for sulfonamidation (Table 1). Initial experimentation indicated that the desired *N*-(4-MeO-phenyl)-*N*-propargylated tolylsulfonamide **I-3a** formed in 45% yield in acetonitrile solvent at 0 °C in the presence of DABCO (5 mol%) (Table 1, entry 1). Altering the solvent to dichloromethane was found to increase yield of **I-3a** to 81% (entry 2). No reaction was observed when omitting DABCO from the reaction (entry 3), thus verifying the need of DABCO. Next, the *ipso*-cyclization was studied using different iodine-based reagent systems. The treatment of **I-3a** with $I_2/NaHCO_3$, independently in toluene and CH_2Cl_2, at −78 °C provided the azaspirocylcohexadienone **3a** in 23% and 31% yields, respectively (entries 4 and 5). The increase in reaction temperature did not help to improve the yields (entry 6). When, the *ipso*-cyclization was carried out in the presence of ICl in toluene at −78 °C, the reaction proceeded well to give **3a** in 58% yield (entry 7). The yield of **3a** improved to 68% in the presence of CH_2Cl_2 (entry 8). To our delight, azaspirocylcohexadienone **3a** was found in 84% yield, under ICl in CH_2Cl_2 at 0 °C for 30 min (entry 9) and lower yield (62%) observed at room temperature. At this point of the examination, we speculated the *ipso*-cyclization can be carried out *in situ* after generation of intermediate **I-3a**. In addition, it was observed that the isolation of *N*-propargylated sulfonamide **I-3a** in high yield was found to be difficult. These findings encouraged us to explore the feasibility of a sequential one-pot synthesis by combining MBH-carbonate **1a**, *N*-(4-methoxyphenyl)-tolylsulfonamide **2a**, DABCO, and then ICl at 0 °C. Indeed, this one-pot reaction progressed smoothly to give **3a** in 81% yield (Table 1, entry 10).

With suitable reaction conditions in hand, we investigated a range of diversely substituted MBH-carbonates with *N*-(4-methoxyphenyl)-tolylsulfonamide **2a** (Scheme 2). It was found that, the MBH-carbonate **1b** having naphthalyl substitution on alkyne functionality reacted well to give azaspirocylcohexadienone **3b** in 82% yield. MBH-carbonates with electron-donating and deficient groups on the phenyl group attached to alkyne were reacted well demonstrating little influence on the *ipso*-cyclization in terms of reaction time and product yield.

The MBH-carbonate bearing aryl substitution with electron-donating groups (4-OMe, 4-Me) took less reaction time for complete conversion to give **3c** (92%) and **3d** (88%). Similarly, 3,5-dimethyl phenyl MBH-carbonate **1e** was also consistent

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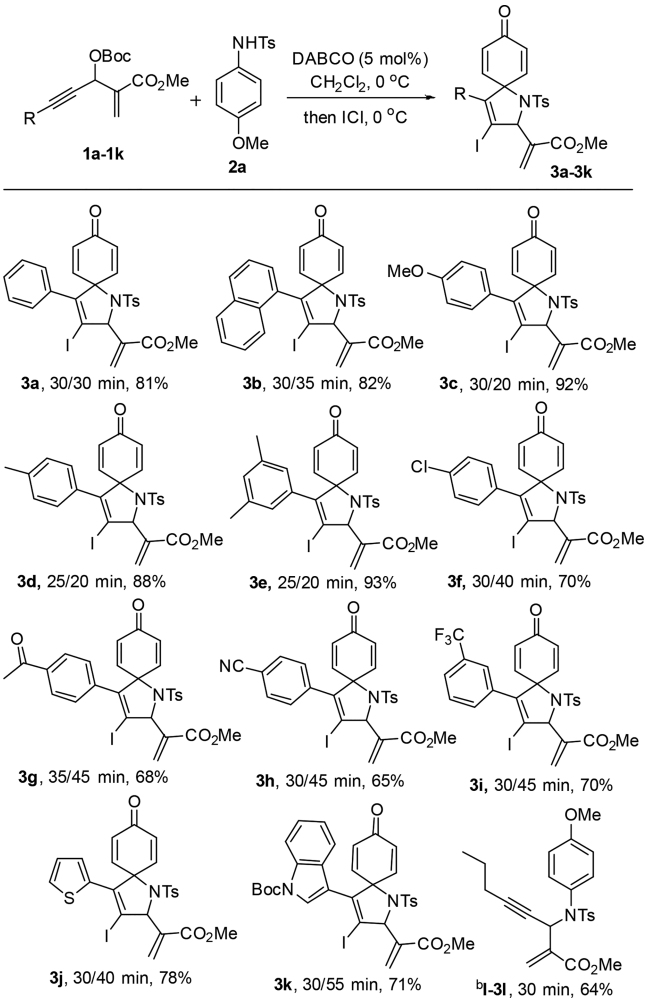
Scheme 2. Scope of MBH-Carbonates[a]

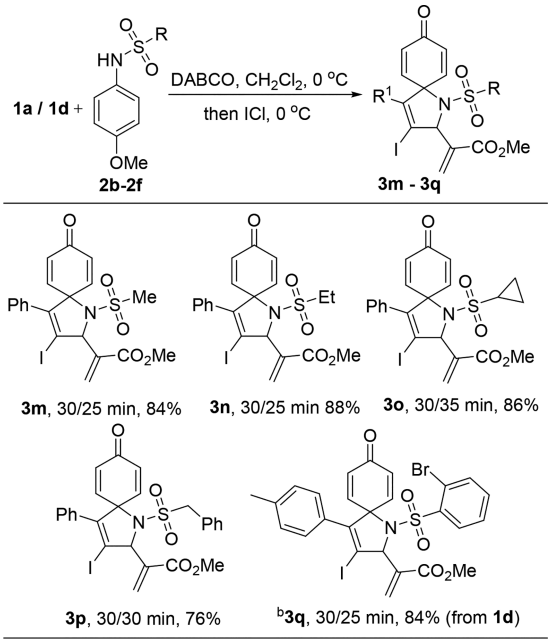


[a]Reaction conditions: MBH-carbonate (1 equiv), *N*-(4-methoxphenyl)-tolylsulfonamide (1.1 equiv) DABCO (5 mol%), CH_2CI_2 (5 mL), 0 °C then ICI (1 equiv) 0 °C. [b]Intermediate **I-3l** was isolated

with optimal reaction conditions and gave **3e** in 93% yield. Substrates **1f–1h** with electron withdrawing groups (4-Cl, 4-$COCH_3$, 4-CN) on phenyl ring required longer reaction times and delivered corresponding products **3f–h** in 65 to 70% yield. 3-Trifluoromethylphenyl group also well tolerated in the reaction of **1i** to give **3i** in 70% yield. MBH-carbonates generated from heteroaryl acetylenic aldehydes **1j** and **1k**, could also be used to prepare the corresponding 3-iodo azaspiro-[4,5]trienones **3j** and **3k** in good yields, although **1k** took prolonged reaction time. The reaction of MBH-carbonate tethered with aliphatic group (**1l**) failed to give the *ipso*-cyclized product, instead intermediate **I-3l** was obtained in 64% yield.

We next set out to explore the scope of *N*-substituted sulfonamides using **1a** as the reaction partner under optimized reaction conditions (Scheme 3). Fascinatingly, the substrate containing *N*-alkyl sulfonamides **2b** (Me), **2c** (Et), **2d** (cyclopropyl) underwent sequential sulfonamidation/*ipso*-cyclization reactions to give spirotrienones **3m**, **3n**, and **3o**, respectively, in good yields. Similarly, *N*-benzyl sulfonamide **2e** could successfully be employed in the reaction to obtain **3p** in 76% yield. Furthermore, the present method was extended to 2-bromo-*N*-(4-methoxyphenyl)benzenesulfonamide **2f** with MBH-carbonate **1d** to furnish the product **3q** in 84% yield.

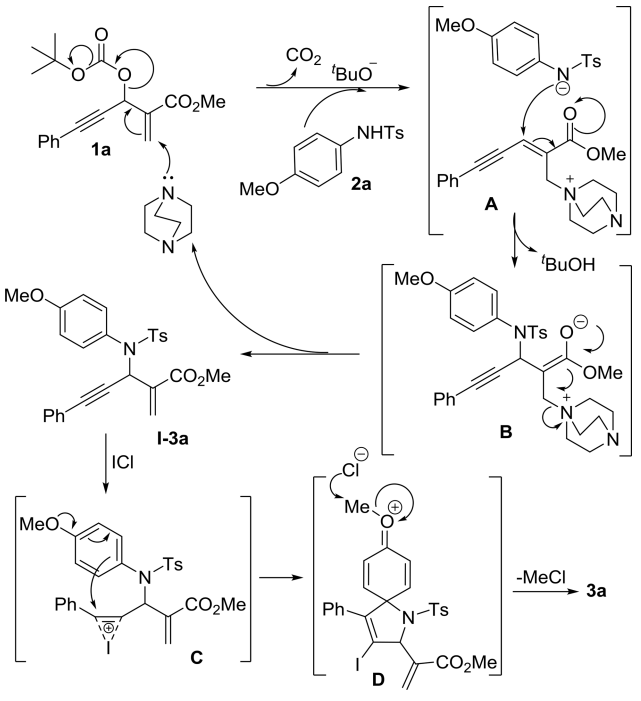
Scheme 3. Scope of Sulfonamides[a]



[a]Reaction conditions: **1a** or **1d** (1 equiv), *N*-(4-methoxphenyl)-sulfonamide (1.1 equiv), DABCO (5 mol%), CH_2CI_2 (5 mL), 0 °C then ICI (1 equiv), 0 °C. [b]Carbonate **1d** used as substrate.

Based on the above results and literature knowledge, a possible reaction pathway for this consecutive sulfonamidation/*ipso*-cyclization is proposed (Scheme 4). Initially, DABCO facilitates the C–N bond formation between **1a** and **2a** to give **I-3a** via intermediates **A** and **B** along with its regeneration.[9] Next, the addition of ICl to **I-3a** allows the formation of iodonium intermediate **C**, which undergoes *ipso*-cyclization to

Scheme 4. Proposed Reaction Mechanism



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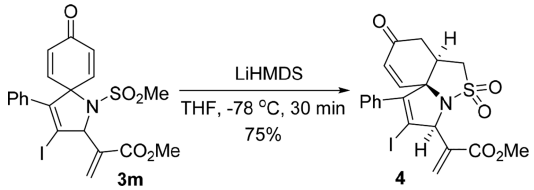
form the desired spirocyclic compound **3a** through spirocyclic intermediate **D**.[5b]

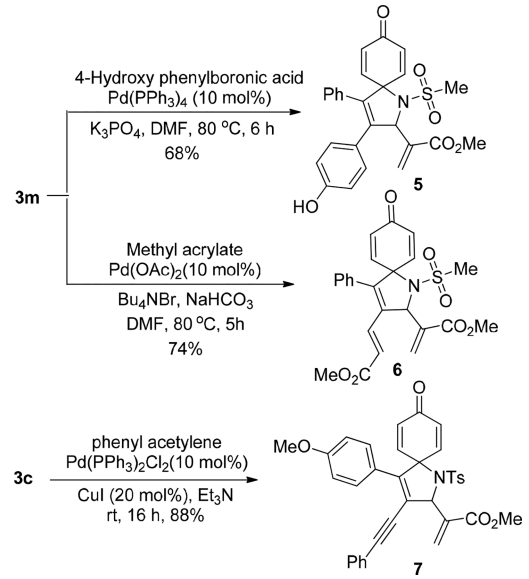
Subsequently, we turned our attention to explore the utility of obtained spirotrienone for the synthesis of sultam (cyclic sulfonamides), privileged scaffold in drug discovery due to its diverse biological activities.[11] In this direction, the spirocyclohexadienone **3m**, bearing *N*-mesyl group, was subjected to stereoselective Michael addition[10] in the presence of LiHMDS to obtain tricyclic-fused sultam derivative **4** in 75% yield (Scheme 5). The stereochemistry of the product was determined by X-ray crystallographic analysis (see the Supporting Information, Figure S1).

Scheme 5. Synthesis of Tricyclic-fused Sultam 4



Finally, further diversification of the *iodo*-spirocyclohexadienone was also studied through Palladium-catalyzed coupling reactions (Scheme 6). In the first case, Suzuki coupling[12a] of

Scheme 6. Diversified Analogues of 3c and 3m



3m with 4-hydroxyphenyl boronic acid gave the coupled product **5** in 68% yield. Likewise, **3m** was subjected to Heck reaction[12b] with methyl acrylate to afford **6** in 74% yield. In addition, the Sonogashira reaction[12c] of **3c** with phenylacetylene in the presence of $PdCl_2(PPh_3)_2$/CuI provided **7** in 88% yield.

CONCLUSION

In conclusion, we have described the first one-pot protocol for the synthesis of azaspirocyclohexadienones via sequential sulfonamidation/*ipso*-cyclization reactions using MBH carbonate and *N*-aryl sulfonamide. This tandem reaction represents a simple and efficient approach to azaspirocyclohexadienones involving sequential C−N, C−I, and C−C bond formations. Usefulness of the spirocyclohexadienones has also been demonstrated to access tricyclic-fused sultam and other diversified derivatives.

EXPERIMENTAL PROCEDURES AND ANALYTICAL DATA

General Information. Reactions were monitored by thin-layer chromatography carried out on silica plates using UV-light and anisaldehyde or *β*-naphthol for visualization. Column chromatography was performed on silica gel (60−120 mesh) using *n*-hexane and ethyl acetate as eluent. Evaporation of solvents was conducted under reduced pressure at temperatures less than 40 °C. FTIR spectra were recorded on KBr thin film. ^{1}H NMR (300, 400, and 500 MHz) and ^{13}C NMR (75, 101, and 126 MHz) spectra were recorded in $CDCl_3$ solvent. Chemical shifts δ and coupling constants J are given in ppm (parts per million) and Hz (hertz), respectively. Chemical shifts are reported relative to residual solvent as an internal standard for ^{1}H and ^{13}C ($CDCl_3$: δ 7.26 ppm for ^{1}H and 77.0 ppm for ^{13}C). Mass spectra were obtained on VG 70-70H or LC/MSD trap SL spectrometer operating at 70 eV using direct inlet system. High-resolution mass spectra (HRMS) [ESI$^+$] were obtained using either a TOF or a double-focusing spectrometer.

General Procedure for the Preparation of MBH-Carbonates, 1a−1k. To a stirred solution of the corresponding MBH-alcohol (1 mmol) in 10 mL of CH_2Cl_2 was added di-*tert*-butyl dicarbonate (0.262 g, 1.2 mmol) and DMAP (6.1 mg, 0.05 mmol) at 0 °C and stirred for given time. After completion of the reaction, the mixture was diluted with water (50 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The crude was purified by flash column chromatography on silica gel (EtOAc: *n*-hexanes) to afford the corresponding MBH-carbonates. All these carbonates were fully characterized and spectral data for new compounds are given below.

*Methyl 3-((tert-Butoxycarbonyl)oxy)-2-methylene-5-(naphthalen-1-yl)pent-4-ynoate (**1b**).* 1.15 g, 84% yield, yellow liquid, R*f* = 0.8 (*n*-hexane:EtOAc = 9:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, J = 8.4 Hz, 1H), 7.85−7.81 (m, 2H), 7.69 (dd, J = 7.1, 1.0 Hz, 1H), 7.57−7.48 (m, 2H), 7.41 (dd, J = 8.2, 7.2 Hz, 1H), 6.58−6.56 (m, 1H), 6.52 (s, 1H), 6.45−6.43 (m, 1H), 3.86−3.81 (m, 3H), 1.54 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.0, 152.3, 136.5, 133.4, 133.1, 130.9, 129.5, 129.4, 128.3, 127.0, 126.5, 126.0, 125.1, 119.5, 88.4, 85.8, 83.2, 65.2, 52.3, 27.8; IR (KBr): ν_{max} = 2984, 1736, 1254, 1151, 1069,953, 850, 781 cm^{-1}; MS (ESI): m/z 389 (M+Na)$^+$; HRMS (ESI): m/z calcd for $C_{22}H_{23}O_5$ (M+H)$^+$: 367.1540; found 367.1540.

*Methyl 3-((tert-Butoxycarbonyl)oxy)-2-methylene-5-(p-tolyl)-pent-4-ynoate (**1d**).* 1.29 g, 90% yield, white solid, R$_f$ = 0.7 (*n*-hexane:EtOAc = 9:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, J = 8.1 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 6.51 (s, 1H), 6.36 (d, J = 9.6 Hz, 2H), 3.81 (s, 3H), 2.35 (s, 3H), 1.52 (d, J = 5.1 Hz, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.9, 152.2, 139.1, 136.5, 131.8, 129.4, 129.1, 129.0, 129.0, 118.8, 87.9, 83.1, 82.8, 64.9, 52.2, 27.7, 21.5; IR (KBr): ν_{max} = 2983, 2232, 1737, 1252, 1150, 1077,951, 813 cm^{-1}; MS (ESI): m/z 353 (M+Na)$^+$; HRMS (ESI): m/z calcd for $C_{19}H_{22}O_5Na$ (M+Na)$^+$: 353.1359, found: 353.1376.

*Methyl 3-((tert-Butoxycarbonyl)oxy)-5-(3,5-dimethylphenyl)-2-methylenepent-4-ynoate (**1e**).* 1.24 g, 88% yield, yellow liquid, R*f* = 0.8 (*n*-hexane:EtOAc = 9:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09 (s, 2H), 6.97 (s, 1H), 6.51 (s, 1H), 6.36 (d, J = 6.8 Hz, 2H), 3.81 (s, 3H), 2.28 (s, 6H), 1.51 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.9, 152.2, 137.8, 136.5, 130.8, 129.6, 129.3, 121.5, 88.1, 83.0, 82.8, 64.9, 52.2, 27.7, 21.0; IR (KBr): ν_{max} = 2981, 2229, 1737, 1255, 1151, 1075,953, 847 cm^{-1}; MS (ESI): m/z 367 (M+Na)$^+$; HRMS (ESI): m/z calcd for $C_{20}H_{24}O_5Na$ (M+Na)$^+$: 367.1516, found: 367.1534.

*Methyl 5-(4-Acetylphenyl)-3-((tert-butoxycarbonyl)oxy)-2-methylenepent-4-ynoate (**1g**).* 0.99 g, 72% yield, yellow liquid, R*f* = 0.4 (*n*-hexane:EtOAc = 9:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82−7.79 (m, 2H), 7.46−7.42 (m, 2H), 6.43 (s, 1H), 6.29 (s, 1H), 6.24 (s, 1H), 3.72 (s, 3H), 2.49 (s, 3H), 1.42 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.0, 164.6, 152.0, 136.7, 136.1, 131.9, 129.2, 128.1, 126.5, 86.7,

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86.5, 83.2, 64.6, 52.2, 27.6, 26.5; IR (KBr): ν_{max} = 2985, 1737, 1685, 1361,1250, 1149, 1078, 953, 843, 751 cm^{-1}; MS (ESI): *m/z* 381 $(M+Na)^+$; HRMS (ESI): *m/z* calcd for $C_{20}H_{22}O_{6Na}$ $(M+Na)^+$: 381.1309, found: 381.1324.

*Methyl 3-((tert-Butoxycarbonyl)oxy)-5-(4-cyanophenyl)-2-methylenepent-4-ynoate (**1h**).* 0.99 g, 70% yield, yellow liquid, R*f* = 0.8 (*n*-hexane:EtOAc = 9:1); ^1H NMR (300 MHz, $CDCl_3$) δ 7.50 (dd, *J* = 23.0, 8.3 Hz, 4H), 6.45 (s, 1H), 6.26 (d, *J* = 21.9 Hz, 2H), 3.74 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.5, 152.0, 136.0, 132.4, 132.0, 129.2, 126.6, 118.1, 112.3, 87.9, 85.6, 83.4, 64.5, 52.3, 27.6; IR (KBr): ν_{max} = 2984, 2230, 1737, 1252, 1150, 1078, 954, 844, 752 cm^{-1}; MS (ESI): *m/z* 364 $(M+Na)^+$; HRMS (ESI): *m/z* calcd for $C_{19}H_{19}NO_5Na$ $(M+Na)^+$: 364.1155, found: 364.1185.

*Methyl 3-((tert-Butoxycarbonyl)oxy)-2-methylene-5-(3-(trifluoromethyl)phenyl)pent-4-ynoate (**1i**).* 0.94 g, 70% yield, yellow liquid, R*f* = 0.8 (*n*-hexane:EtOAc = 9:1); ^1H NMR (400 MHz, CDCl3) δ 7.65 (s, 1H), 7.54 (dd, *J* = 14.6, 7.8 Hz, 2H), 7.38 (t, *J* = 7.8 Hz, 1H), 6.46 (s, 1H), 6.30 (d, *J* = 0.8 Hz, 1H), 6.26 (s, 1H), 3.75 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.7, 152.1, 136.2, 135.0, 129.3, 128.8, 128.7, 125.5, 122.8, 85.9, 85.2, 83.4, 64.6, 52.3, 27.7; IR (KBr): ν_{max} = 2925,1737,1256, 1132, 1079, 956, 801, 694 cm^{-1}; MS (ESI): *m/z* 407 $(M+Na)^+$; HRMS (ESI): *m/z* calcd for $C_{19}H_{19}F_3O_5Na$ $(M+Na)^+$: 407.1077, found: 407.1099.

General Procedure for the Preparation of 3a−3k. To a solution of MBH carbonate **1a** to **1k** (1 mmol) and *N*-(4-methoxyphenyl)-4-methylbenzenesulfonamide **2a** (1.1 mmol) in 5 mL of CH_2Cl_2 was added DABCO (5 mol%) at 0 °C and stirred up to 30 min. Then, ICl (1 mmol) was added dropwise to the reaction mixture at 0 °C. After the completion of reaction (monitored by TLC), saturated aqueous $Na_2S_2O_3{\cdot}5H_2O$ solution (10 mL) was added to the reaction mixture and extracted with CH_2Cl_2 (2 × 10 mL), washed with brine (2 × 10 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue obtained was purified by column chromatography on silica gel (EtOAc:hexanes) to afford the corresponding spirocyclohexadienones **3a** to **3k**.

*Methyl 3-((N-(4-Methoxyphenyl)-4-methylphenyl)sulfonamido)-2-methylene-5-phenylpent-4-ynoate (**I-3a**).* 234 mg, 81% yield, yellow solid, mp: 119−120 °C, R*f* = 0.6 (*n*-hexane:EtOAc = 9:1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.68−7.62 (m, 2H), 7.36−7.28 (m, 3H), 7.27−7.21 (m, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.02−6.97 (m, 2H), 6.76−6.71 (m, 2H), 6.58 (s, 1H), 6.21 (s, 1H), 5.78 (d, *J* = 1.9 Hz, 1H), 3.89 (s, 3H), 3.76 (s, 3H), 2.36 (s, 3H);^{13}C NMR (101 MHz, $CDCl_3$) δ 165.4, 159.6, 143.2, 136.6, 136.4, 131.4, 129.0, 128.7, 128.4, 128.3, 122.0, 113.8, 88.4, 84.6, 55.3, 52.4, 52.1, 21.5; IR (KBr): ν_{max} = 2952, 1726, 1505, 1348, 1247, 1159, 1029, 752, 665 cm-1; MS (ESI): *m/z* 498 $(M+Na)^+$; HRMS (ESI): *m/z* calcd for $C_{27}H_{26}NO_5S$ $(M+H)^+$: 476.1526, found: 476.1534.

*Methyl 2-(3-Iodo-8-oxo-4-phenyl-1-tosyl-1-azaspiro[4.5]deca-3,6,9-trien-2-yl)acrylate (**3a**).* 300 mg, 81% yield, white solid, mp: 206−208 °C, R*f* = 0.3 (*n*-hexane:EtOAc = 9:1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.2 Hz, 2H), 7.36−7.29 (m, 4H), 7.27 (d, *J* = 2.1 Hz, 1H), 7.18 (dd, *J* = 10.1, 2.8 Hz, 1H), 7.07−6.98 (m, 2H), 6.86 (dd, *J* = 9.9, 2.6 Hz, 1H), 6.56 (s, 1H), 6.20 (dd, *J* = 10.0, 1.9 Hz, 1H), 6.13 (dd, *J* = 10.8, 2.6 Hz, 2H), 5.56 (s, 1H), 3.68 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.5, 164.4, 147.6, 147.5, 144.0, 144.0, 136.9, 132.9, 132.6, 129.8, 129.4, 129.4, 129.1, 128.2, 128.1, 97.7, 74.5, 51.8, 21.6; IR (KBr): 3020, 2925, 2854, 1667, 1350, 1160, 1073, 764, 664 cm^{-1}; MS (ESI): *m/z* 610 $(M+Na)^+$; HRMS (ESI): *m/z* calcd for $C_{26}H_{22}INO_5SNa$ $(M+Na)^+$: 610.0156, found: 610.0189.

*Methyl 2-(3-Iodo-4-(naphthalen-1-yl)-8-oxo-1-tosyl-1-azaspiro[4.5]deca-3,6,9-trien-2-yl)acrylate (**3b**).* 285 mg, 82% yield, white solid, mp: 208−210 °C, R*f* = 0.5 (*n*-hexane:EtOAc = 7:3); ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.9 Hz, 1H), 7.83−7.77 (m, 2H), 7.68 (d, *J* = 8.3 Hz, 2H), 7.49−7.44 (m, 2H), 7.36−7.27 (m, 4H), 7.06−6.97 (m, 2H), 6.56 (s, 1H), 6.27 (dd, *J* = 10.0, 2.0 Hz, 1H), 6.15 (s, 1H), 5.76 (dd, *J* = 10.1, 2.0 Hz, 1H), 5.58 (s, 1H), 3.70 (d, *J* = 5.7 Hz, 3H), 2.45 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.4, 164.3, 147.6, 147.2, 144.1, 143.1, 136.8, 133.4, 131.5, 129.7, 129.4, 129.2, 128.5, 128.5, 128.3, 126.6, 126.0, 125.6, 124.3, 100.7, 75.9, 75.2, 51.8, 21.6; IR (KBr): 3017, 2953, 1720, 1667, 1343, 1163, 1091, 753, 668 cm^{-1}; MS (ESI): *m/z* 660 $(M+Na)^+$: HRMS (ESI): *m/z* calcd for $C_{30}H_{25}INO_5S$ $(M+H)^+$: 638.0493, found: 638.0473.

*Methyl 2-(3-Iodo-4-(4-methoxyphenyl)-8-oxo-1-tosyl-1-azaspiro[4.5]deca-3,6,9-trien-2-yl)acrylate (**3c**).* 328 mg, 92% yield, yellow semi solid, R*f* = 0.4 (*n*-hexane:EtOAc = 7:3); ^1H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 5.4 Hz, 2H), 7.13 (d, *J* = 8.1 Hz, 1H), 6.93 (d, *J* = 8.6 Hz, 2H), 6.79 (dd, *J* = 17.5, 9.1 Hz, 3H), 6.52 (s, 1H), 6.21−6.05 (m, 3H), 5.52 (s, 1H), 3.77 (s, 3H), 3.65 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.6, 164.5, 159.9, 194.4, 147.9, 147.8, 144.0, 143.6, 136.8, 132.9, 130.6, 129.8, 129.4, 129.8, 128.2, 124.7, 113.5, 97.9, 74.4, 74.1, 55.1, 51.8, 21.6; IR (KBr): 3015, 2951, 2843, 1727, 1665, 1343, 1247, 1161, 750, 664 cm^{-1}; MS (ESI): *m/z* 640 $(M+Na)^+$; HRMS (ESI): *m/z* calcd for $C_{27}H_{24}INO_6SNa$ $(M+Na)^+$: 640.0261, found: 640.0259.

*Methyl 2-(3-Iodo-8-oxo-4-(p-tolyl)-1-tosyl-1-azaspiro[4.5]deca-3,6,9-trien-2-yl)acrylate (**3d**).* 320 mg, 88% yield, pale yellow solid, mp: 156−158 °C, R*f* = 0.5 (*n*-hexane:EtOAc = 7:3); ^1H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.1 Hz, 2H), 7.29−7.24 (m, 2H), 7.14 (dd, *J* = 10.0, 2.6 Hz, 1H), 7.06 (d, *J* = 7.9 Hz, 2H), 6.87 (d, *J* = 8.0 Hz, 2H), 6.81 (d, *J* = 8.2 Hz, 1H), 6.53 (s, 1H), 6.17 (dd, *J* = 10.0, 1.8 Hz, 1H), 6.13−6.06 (m, 2H), 5.52 (s, 1H), 3.65 (s, 3H), 2.43 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.6, 164.5, 147.8, 147.6, 144.0, 144.0, 139.0, 136.9, 132.9, 129.7,129.6, 129.4, 129.2, 129.1, 128.8, 128.2, 97.6, 74.4, 74.3, 51.8, 21.6, 21.3; IR (KBr): 3022, 2952, 1724, 1665, 1445, 1156, 1034, 748, 664 cm^{-1}; MS (ESI): *m/z* 624 $(M+Na)^+$; HRMS (ESI): *m/z* calcd for $C_{27}H_{25}INO_5S$ $(M+H)^+$: 602.0493, found: 602.0480.

*Methyl 2-(4-(3,5-Dimethylphenyl)-3-iodo-8-oxo-1-tosyl-1-azaspiro[4.5]deca-3,6,9-trien-2-yl)acrylate (**3e**).* 332 mg, 93% yield, white solid, mp: 149−151 °C, R*f* = 0.5 (*n*-hexane:EtOAc = 7:3); ^1H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.3 Hz, 2H), 7.29−7.23 (m, 2H), 7.14 (dd, *J* = 10.0, 2.5 Hz, 1H), 6.91 (s, 1H), 6.78 (dd, *J* = 15.3, 5.9 Hz, 1H), 6.55 (d, *J* = 19.6 Hz, 3H), 6.19−6.06 (m, 3H), 5.52 (s, 1H), 3.66 (s, 3H), 2.43 (s, 3H), 2.23 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.7, 164.5, 147.8, 147.6, 144.2, 144.0, 137.4, 137.1, 136.9, 132.7, 132.4, 130.8 129.7, 129.4, 129.0, 128.2, 126.9, 97.3, 74.4, 74.1, 51.8, 21.5, 21.2; IR (KBr): 3017, 2922, 2857, 1720, 1667, 1445, 1344, 1160, 1091, 754, 667 cm^{-1}; MS (ESI): *m/z* 638 $(M+Na)^+$; HRMS (ESI): *m/z* calcd for $C_{28}H_{26}INO_5SNa$ $(M+Na)^+$: 638.0469, found: 638.0475.

*Methyl 2-(4-(4-Chlorophenyl)-3-iodo-8-oxo-1-tosyl-1-azaspiro[4.5]deca-3,6,9-trien-2-yl)acrylate (**3f**).* 248 mg, 70% yield, yellow solid, mp: 194−196 °C, R*f* = 0.4 (*n*-hexane:EtOAc = 7:3); ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.3 Hz, 2H), 7.29−7.27 (m, 2H), 7.26−7.23 (m, 2H), 7.14 (dd, *J* = 10.0, 3.0 Hz, 1H), 6.99−6.92 (m, 2H), 6.84 (dd, *J* = 10.0, 2.7 Hz, 1H), 6.52 (s, 1H), 6.19 (dd, *J* = 10.0, 2.0 Hz, 1H), 6.12 (dd, *J* = 10.1, 2.0 Hz, 1H), 6.09 (s, 1H), 5.50 (s, 1H), 3.63 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.4, 164.3, 147.4, 147.4, 144.1, 142.8, 136.8, 135.3, 133.2, 131.0, 130.8, 130.0, 129.4, 129.1, 128.5, 128.2, 98.4, 74.6, 74.4, 51.7, 21.6; IR (KBr): 2924, 2855, 1719, 1666, 1445, 1343, 1160, 1087, 753, 667 cm^{-1}; MS (ESI): *m/z* 644 $(M+Na)^+$; HRMS (ESI): *m/z* calcd for $C_{26}H_{21}ClINO_5SNa$ $(M+Na)^+$: 643.9766, found: 643.9770.

*Methyl 2-(4-(4-Acetylphenyl)-3-iodo-8-oxo-1-tosyl-1-azaspiro[4.5]deca-3,6,9-trien-2-yl)acrylate (**3g**).* 238 mg, 68% yield, pale yellow liquid, R*f* = 0.3 (*n*-hexane:EtOAc = 7:3); ^1H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.2 Hz, 2H), 7.65 (d, *J* = 8.2 Hz, 2H), 7.29−7.27 (m, 2H), 7.20−7.10 (m, 3H), 6.88 (dd, *J* = 9.9, 2.4 Hz, 1H), 6.53 (s, 1H), 6.19 (dd, *J* = 10.0, 1.9 Hz, 1H), 6.14−6.09 (m, 2H), 5.52 (s, 1H), 3.64 (s, 3H), 2.57 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.3, 184.3, 164.3, 147.4, 147.2, 144.2, 143.0, 137.4, 137.3, 136.8, 133.4, 130.0, 129.8, 129.4, 129.1, 128.2, 128.0, 98.3, 74.8, 74.5, 51.8, 26.6, 21.6; IR (KBr): 2985, 1737, 1685, 1361, 1249, 1149, 1077, 952, 843, 751, 639 cm^{-1}; MS (ESI): *m/z* 652 $(M+Na)^+$; HRMS (ESI): *m/z* calcd for $C_{28}H_{24}INO_6SNa$ $(M+Na)^+$: 652.0261 found: 652.0243.

*Methyl 2-(4-(4-Cyanophenyl)-3-iodo-8-oxo-1-tosyl-1-azaspiro[4.5]deca-3,6,9-trien-2-yl)acrylate (**3h**).* 232 mg, 65% yield, yellow solid, mp: 194−196 °C, R*f* = 0.4 (*n*-hexane:EtOAc = 7:3); ^1H NMR (300 MHz, $CDCl_3$) δ 7.61 (dd, *J* = 13.9, 8.2 Hz, 4H), 7.28 (d, *J*

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= 6.4 Hz, 2H), 7.17 (dd, *J* = 9.8, 5.6 Hz, 3H), 6.89 (dd, *J* = 10.0, 2.7 Hz, 1H), 6.53 (s, 1H), 6.25−6.07 (m, 3H), 5.50 (s, 1H), 3.62 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.1, 164.2, 147.2, 146.9, 144.2, 142.2, 137.5, 136.7, 136.0, 133.7, 132.0, 130.4, 130.1, 129.5, 129.2, 128.2, 118.1, 113.2, 99.0, 75.4, 74.4, 51.8, 21.6; IR (KBr): 3018, 2953, 2231, 1720, 1668, 1344, 1163, 1090, 849, 757, 668 cm^{-1}; MS (ESI): *m*/*z* 635 $(M+Na)^+$; HRMS (ESI): *m*/*z* calcd for $C_{27}H_{21}IN_2O_5SNa$ $(M+Na)^+$: 635.0108 found: 635.0127.

Methyl 2-(3-Iodo-8-oxo-1-tosyl-4-(3-(trifluoromethyl)phenyl)-1-azaspiro[4.5]deca-3,6,9-trien-2-yl)acrylate (**3i**). 238 mg, 70% yield, pale yellow solid, mp:168−170 °C, R*f* = 0.3 (*n*-hexane:EtOAc = 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.3 Hz, 2H), 7.58 (d, *J* = 7.9 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.31−7.25 (m, 3H), 7.24−7.16 (m, 2H), 6.88 (dd, *J* = 10.0, 2.8 Hz, 1H), 6.53 (s, 1H), 6.22−6.08 (m, 3H), 5.52 (s, 1H), 3.64 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.2, 164.3, 147.3, 147.2, 144.2, 142.5, 136.8, 136.4, 133.5, 132.8, 130.8, 130.4, 130.1, 129.4, 129.2, 128.7, 128.2, 126.4, 126.4, 125.9, 125.9, 124.9, 122.2, 99.0, 74.7, 74.4, 51.8, 21.5; IR (KBr): 2924, 2855, 1721, 1669, 1335, 1164, 1089, 755, 668 cm^{-1}; MS (ESI): *m*/*z* 678 $(M+Na)^+$; HRMS (ESI): *m*/*z* calcd for $C_{27}H_{22}F_3INO_5S$ $(M+H)^+$: 656.0210 found: 656.0206.

Methyl 2-(3-Iodo-8-oxo-4-(thiophen-2-yl)-1-tosyl-1-azaspiro[4.5]deca-3,6,9-trien-2-yl)acrylate (**3j**). 287 mg, 78% yield, white solid; mp: 182−184 °C, R*f* = 0.4 (*n*-hexane:EtOAc = 7:3); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.3 Hz, 2H), 7.25−7.19 (m, 3H), 7.03 (dd, *J* = 10.1, 2.7 Hz, 1H), 6.95 (dd, *J* = 3.6, 1.2 Hz, 1H), 6.89 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.70 (d, *J* = 7.1 Hz, 1H), 6.47 (s, 1H), 6.18 (ddd, *J* = 21.2, 10.0, 2.0 Hz, 2H), 6.01 (s, 1H), 5.47 (s, 1H), 3.59 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.7, 164.5, 147.5, 147.3, 147.3, 144.1, 137.2, 136.7, 132.9, 132.2, 130.5, 129.6, 129.4, 128.3, 127.7, 126.8, 99.6, 74.4, 73.7, 51.8, 21.6; IR (KBr): 2924, 2855,, 1720, 1669, 1344, 1160, 1088, 753, 666 cm^{-1}; MS (ESI): *m*/*z* 616 $(M+Na)^+$; HRMS (ESI): *m*/*z* calcd for $C_{24}H_{20}INO_5S_2Na$ $(M+Na)^+$: 615.9720, found: 615.9724.

tert-Butyl3-(3-iodo-2-(3-methoxy-3-oxoprop-1-en-2-yl)-8-oxo-1-tosyl-1-azaspiro[4.5]deca-3,6,9-trien-4-yl)-1H-indole-1-carboxylate (**3k**). 226 mg, 71% yield, reddish brown solid, mp: 104−106 °C, R*f* = 0.2 (*n*-hexane:EtOAc = 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.9 Hz, 1H), 7.59 (d, *J* = 8.3 Hz, 2H), 7.40−7.29 (m, 1H), 7.26 (s, 1H), 7.25−7.22 (m, 1H), 7.22−7.17 (m, 3H), 7.15−7.07 (m, 2H), 6.89−6.76 (m, 1H), 6.47 (s, 1H), 6.15−5.94 (m, 2H), 5.49 (s, 1H), 3.58 (s, 3H), 2.36 (s, 3H), 1.58 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.7, 164.3, 149.1, 147.5, 147.3, 144.1, 136.9, 134.6, 133.2, 129.4, 128.5, 128.2, 124.8, 122.8, 120.5, 115.3, 112.0, 100.3, 84.5, 75.2, 51.8, 28.1, 21.6; IR (KBr): 2985, 1727, 1667, 1363, 1363, 1155, 753, 668 cm^{-1}; MS (ESI): *m*/*z* 749 $(M+Na)^+$; HRMS (ESI): *m*/*z* calcd for $C_{33}H_{31}IN_2O_7SNa$ $(M+Na)^+$: 749.0789, found: 749.0770.

Methyl 3-(N-(4-Methoxyphenyl)-4-methylphenylsulfonamido)-2-methyleneoct-4-ynoate (**I-3l**). 200 mg, 64%, pale yellow solid, mp: 85−87 °C ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (t, *J* = 12.5 Hz, 2H), 7.23 (t, *J* = 10.7 Hz, 2H), 6.90 (t, *J* = 13.7 Hz, 2H), 6.71 (d, *J* = 8.9 Hz, 2H), 6.34 (s, 1H), 6.14 (s, 1H), 5.70 (s, 1H), 3.85 (s, 3H), 3.76 (s, 3H), 2.41 (s, 3H), 2.11 (td, *J* = 7.0, 2.0 Hz, 2H), 1.52−1.37 (m, 2H), 0.92 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.6, 159.5, 143.0, 137.0, 132.6, 130.4, 128.8, 128.4, 128.2, 113.6, 89.0, 75.6, 55.2, 52.2, 51.8, 21.7, 21.5, 20.6, 13.5. IR (KBr): 2961, 2230, 1727, 1507, 1350, 1163, 1033, 750 cm-1; MS (ESI): *m*/*z* 464 $(M+Na)^+$; HRMS (ESI): *m*/*z* calcd for $C_{24}H_{28}NO_5S$ $(M+H)^+$: 442.1688 found: 442.1689.

General Procedure for the Preparation of 3m−3q. To a solution of **1a**/**1d** (1 mmol) and *N*-(4-methoxyphenyl)-methanesulfonamide (**2b−f**) (1.1 mmol) in 5 mL of CH_2Cl_2 was added DABCO (5.60 mg, 0.05 mmol) at 0 °C and stirred up to 30 min. Then, ICl (162.3 mg, 1 mmol) was added dropwise to the reaction mixture at 0 °C. After the completion of reaction (monitored by TLC), saturated aqueous $Na_2S_2O_3{\cdot}5H_2O$ solution (10 mL) was added to the reaction mixture and extracted with CH_2Cl_2 (2 × 10 mL), washed with brine (2 × 10 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue obtained was purified by column chromatography on silica gel (EtOAc:hexanes) to afford **3m−q**.

Methyl 2-(3-Iodo-1-(methylsulfonyl)-8-oxo-4-phenyl-1-azaspiro[4.5]deca-3,6,9-trien-2-yl)acrylate (**3m**). 271 mg, 84% yield, yellow solid, mp: 194−196 °C, R*f* = 0.6 (*n*-hexane:EtOAc = 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.20 (m, 4H), 6.99 (dt, *J* = 3.8, 2.2 Hz, 2H), 6.89 (dd, *J* = 10.0, 3.0 Hz, 1H), 6.60 (s, 1H), 6.11 (ddd, *J* = 12.0, 10.0, 2.6 Hz, 3H), 5.49 (s, 1H), 3.79 (s, 3H), 2.81 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.3, 164.9, 148.1, 145.7, 144.4, 135.8, 135.0, 132.5, 130.9, 129.3, 129.2, 128.7, 128.2, 96.5, 75.0, 73.9, 52.2, 42.6; IR (KBr): 3022, 2952, 1720, 1666, 1340, 1155, 1083, 857, 753, 704 cm^{-1}; MS (ESI): *m*/*z* 534 $(M+Na)^+$; HRMS (ESI): *m*/*z* calcd for $C_{20}H_{18}INO_5SNa$ $(M+Na)^+$: 533.9843 found: 533.9877.

Methyl 2-(1-(Ethylsulfonyl)-3-iodo-8-oxo-4-phenyl-1-azaspiro[4.5]deca-3,6,9-trien-2-yl)acrylate (**3n**). 292 mg, 88% yield, pale yellow semi solid, R$_f$ = 0.6 (*n*-hexane:EtOAc = 7:3); ^{1}H NMR (500 MHz, CDCl3) δ 7.35−7.24 (m, 4H), 7.11−7.03 (m, 2H), 7.03−6.98 (m, 1H), 6.63 (s, 1H), 6.18−6.12 (m, 3H), 5.58 (s, 1H), 3.85 (s, 3H), 3.08−2.84 (m, 2H), 1.30 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.4, 164.8, 148.2, 146.3, 144.2, 136.2, 136.6, 132.6, 130.5, 129.4, 129.1, 128.4, 128.1, 96.7, 75.0, 74.1, 52.2, 49.6, 7.9; IR (KBr): 2994, 2253, 1720, 1665, 1336, 1148, 1045, 912, 856, 780, 727, 643 cm^{-1}; MS (ESI): *m*/*z* 548 $(M+Na)^+$; HRMS (ESI): *m*/*z* calcd for $C_{21}H_{20}NO_5SINa$ $(M+Na)^+$: 548.0006 found: 548.0005.

Methyl 2-(1-(Cyclopropylsulfonyl)-3-iodo-8-oxo-4-phenyl-1-azaspiro[4.5]deca-3,6,9-trien-2-yl)acrylate (**3o**). 292 mg, 86% yield, pale yellow semi solid, R*f* = 0.4 (*n*-hexane:EtOAc = 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.27 (m, 4H), 7.06 (dt, *J* = 3.9, 2.3 Hz, 2H), 7.02−6.97 (m, 1H), 6.64 (s, 1H), 6.15 (d, *J* = 9.9 Hz, 3H), 5.58 (s, 1H), 3.85 (s, 3H), 2.39−2.30 (m, 1H), 1.20−1.10 (m, 2H), 0.98−0.90 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.5, 164.8, 148.3, 147.3, 144.2, 137.1, 134.0, 132.7, 130.1, 129.4, 129.1, 128.6, 128.1, 97.1, 74.8, 74.1, 52.1, 32.3, 6.6, 6.4; IR (KBr): 33018, 2358, 1720, 1666, 1340, 1151, 1042, 858, 701 cm^{-1}; MS (ESI): *m*/*z* 560 $(M+Na)^+$; HRMS (ESI): *m*/*z* calcd for $C_{22}H_{20}NO_5SINa$ $(M+Na)^+$: 560.0013 found: 560.0005.

Methyl 2-(1-(Benzylsulfonyl)-3-iodo-8-oxo-4-phenyl-1-azaspiro[4.5]deca-3,6,9-trien-2-yl)acrylate (**3p**). 282 mg, 76% yield, pale yellow, Semi solid, R*f* = 0.4 (*n*-hexane:EtOAc = 7:3); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41−7.23 (m, 9H), 7.02 (d, *J* = 7.3 Hz, 2H), 6.86−6.75 (m, 1H), 6.66 (s, 1H), 6.13 (s, 1H), 6.08 (d, *J* = 10.0 Hz, 1H), 5.98 (d, *J* = 10.0 Hz, 1H), 5.51 (s, 1H), 4.22−4.13 (m, 2H), 3.87 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.4, 164.87, 147.8, 146.1, 144.3, 136.2, 134.7, 132.6, 131.0, 130.0, 129.4, 127.1, 129.0, 128.7, 128.6, 128.1, 128.0, 96.4, 75.0, 74.2, 61.0, 52.2; IR (KBr): 3059, 2951, 2253, 1720, 166, 1626, 1345, 1154, 1078, 731, 700, 646 cm^{-1}; MS (ESI): *m*/*z* 610 $(M+Na)^+$; HRMS (ESI): *m*/*z* calcd for $C_{26}H_{22}NO_5SINa$ $(M+Na)^+$: 610.0169 found: 610.0161.

Methyl 2-(1-((2-Bromophenyl)sulfonyl)-3-iodo-8-oxo-4-(p-tolyl)-1-azaspiro[4.5]deca-3,6,9-trien-2-yl)acrylate (**3q**). 339 mg, 84% yield, pale yellow, Semi solid; R*f* = 0.4 (*n*-hexane:EtOAc = 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 7.8, 1.9 Hz, 1H), 7.70 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.42−7.28 (m, 3H), 7.06 (d, *J* = 7.8 Hz, 2H), 6.90 (d, *J* = 8.1 Hz, 2H), 6.86 (dd, *J* = 10.1, 3.0 Hz, 1H), 6.38 (s, 1H), 5.99 (dd, *J* = 10.2, 2.0 Hz, 1H), 5.95 (s, 1H), 5.91 (dd, *J* = 10.1, 2.0 Hz, 1H), 5.84 (s, 1H), 3.80 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.3, 164.8, 148.0, 146.3, 143.7, 139.1, 137.9, 137.1, 135.5, 134.8, 133.9, 132.2, 129.4, 129.2, 128.8, 127.5, 121.9, 97.7, 74.9, 73.7, 52.0, 21.3; IR (KBr): 2950, 2922, 2252, 1721, 166, 1438, 1334, 1161, 1030, 911, 729, 620 cm^{-1}; MS(ESI): *m*/*z* 690 $(M+Na)^+$; HRMS (ESI): *m*/*z* calcd for $C_{26}H_{21}BrINO_5SNa$ $(M+Na)^+$ 687.9266 found: 687.9267.

Methyl 2-(2-Iodo-5,5-dioxido-8-oxo-1-phenyl-6,6a,7,8-tetrahydro-3H-benzo[c]pyrrolo[1,2-b]isothiazol-3-yl)acrylate (**4**). LHMDS in THF (0.3 mL 1 M solution in THF, 1.5 mmol) was added to a solution of **3m** (100 mg, 1 mmol) in THF (5 mL) at −78 °C. The progress of the conversion was monitored by TLC. Upon completion of the reaction, the mixture was warmed to 0 °C, neutralized with aq. saturated NH_4Cl (3 mL) and extracted with EtOAc (2 × 10 mL). The combined extracts were sequentially washed with aq. saturated NH_4Cl

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(2 × 10 mL) and brine (2 × 10 mL), dried (Na_2SO_4), and evaporated. The residue was dried (high vacuum) and chromatographed (5% EtOAc) to give 75 mg of **4**.

75 mg, 75% yield, pale yellow solid, mp: 85−87 °C; R*f* = 0.5 (*n*-hexane:EtOAc = 4:6); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44−7.38 (m, 3H), 7.24−7.18 (m, 2H), 7.08 (dd, *J* = 10.3, 1.5 Hz, 1H), 6.56 (s, 1H), 6.19−6.06 (m, 2H), 5.66 (s, 1H), 3.84−3.82 (m, 3H), 3.51 (dd, *J* = 12.0, 5.9 Hz, 1H), 3.37−3.22 (m, 2H), 2.30 (dt, *J* = 16.5, 3.6 Hz, 1H), 1.97 (dd, *J* = 17.4, 5.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.8, 164.8, 146.4, 146.1, 137.2, 133.3, 132.3, 129.5, 129.5, 129.0, 128.6, 95.8, 78.7, 71.1, 53.5, 52.1, 41.1, 36.4; IR (KBr): 2924, 2359, 1722, 1682, 1314, 1149, 1075, 766, 731, 704 cm^{-1}; MS (ESI): *m*/*z* 534 (M+Na)$^+$; HRMS (ESI): *m*/*z* calcd for $C_{20}H_{19}INO_5S$ (M+H)$^+$: 512.0023 found: 512.0011.

Methyl 2-(3-(4-Hydroxyphenyl)-1-(methylsulfonyl)-8-oxo-4-phenyl-1-azaspiro[4.5]deca-3,6,9-trien-2-yl)acrylate (5). To a solution of **3m** (100 mg, 0.195 mmol), K_3PO_4 (165 mg, 0.78 mmol), $Pd(PPh_3)_4$ (10 mol%), and (4- hydroxyphenyl)boronic acid (41 mg, 0.29 mmol) in DMF (5 mL) was degassed with N_2 for 20 min. The reaction mixture was heated at 80 °C for 6 h. After the completion of reaction, DMF was removed under vacuum, and the residue was dissolved in EtOAc (5 mL), filtered through Celite, and concentrated *in vacuo*. The crude was purified by column chromatography on silica gel (EtOAc in *n*-hexane) to afford **5**.

63 mg, 68% yield, yellow semi solid, R_f = 0.3 (*n*-hexane:EtOAc = 7:3); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (dd, *J* = 10.1, 2.9 Hz, 1H), 7.22−7.14 (m, 3H), 7.00 (dd, *J* = 7.9, 1.5 Hz, 2H), 6.92 (dd, *J* = 10.1, 2.9 Hz, 1H), 6.87−6.82 (m, 2H), 6.58−6.52 (m, 2H), 6.40 (s, 1H), 6.33 (dd, *J* = 10.1, 2.0 Hz, 1H), 6.13−5.99 (m, 3H), 5.79 (s, 1H), 3.73 (s, 3H), 2.93 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.0, 165.7, 155.9, 149.8, 147.7, 133.7, 132.5, 131.8, 130.5, 130.2, 130.1, 128.4, 128.3, 128.1, 124.1, 115.2, 74.0, 69.6, 52.1, 42.4; IR (KBr): 3414, 3022, 2953, 1720, 1665, 1516, 1441, 1338, 1154, 956, 796, 753, 699 cm^{-1}; MS (ESI): *m*/*z* 500 (M+Na)$^+$; HRMS (ESI): *m*/*z* calcd for $C_{26}H_{23}NO_6S$ (M+Na)$^+$: 500.1138 found: 500.1113.

(E)-Methyl-2-(3-(3-methoxy-3-oxoprop-1-en-1-yl)-1-(methylsulfonyl)-8-oxo-4-phenyl-1-azaspiro[4.5]deca-3,6,9-trien-2-yl) Acrylate (6). To a solution of **3m** (100 mg, 0.196 mmol), $Pd(OAc)_2$ (5 mg, 0.196 mmol, 10 mol%), Bu_4NBr (63 mg, 0.196 mmol), $NaHCO_3$ (41 mg, 0.49 mmol), and methyl acrylate (19 mg, 0.216 mmol) in DMF (5 mL). The reaction mixture was heated at 80 °C for 5 h. After the completion, reaction was quenched by aqueous NH_4Cl (10 mL). The mixture was extracted with EtOAc (2 × 5 mL) organic layer was washed with H_2O (5 mL) followed by brine (5 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The crude was purified by column chromatography on silica gel (EtOAc in *n*-hexane) to afford **6**.

67.5 mg, 74% yield, yellow solid, mp: 98−100 °C, R_f = 0.5 (*n*-hexane:EtOAc = 7:3); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38−7.25 (m, 5H), 7.10−7.06 (m, 2H), 7.03−6.99 (m, 1H), 6.90 (dd, J = 10.0, 3.0 Hz, 1H), 6.62 (s, 1H), 6.29−6.22 (m, 2H), 6.15 (dd, J = 10.0, 1.8 Hz, 1H), 5.87 (dd, J = 9.1, 7.2 Hz, 2H), 3.83 (s, 3H), 3.67 (s, 3H), 2.90 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.2, 166.4, 165.3, 148.5, 145.6, 145.3, 135.0, 131.2, 129.7, 129.5, 128.9, 128.2, 122.1, 73.4, 67.8, 52.3, 51.8, 42.8; IR (KBr): 3021, 2952, 1716, 1667, 1438, 1342, 1155, 969, 755, 700 cm^{-1}; MS (ESI): *m*/*z* 492 (M+Na)$^+$; HRMS (ESI): *m*/*z* calcd for $C_{24}H_{24}NO_7S$ (M+H)$^+$: 470.1268 found: 470.1298.

Methyl 2-(4-(4-Methoxyphenyl)-8-oxo-3-(phenylethynyl)-1-tosyl-1-azaspiro[4.5]deca-3,6,9-trien-2-yl)acrylate (7). To a solution of **3c** (100 mg, 0.25 mmol) in triethylamine (3 mL) was added to a mixture of $Pd(PPh_3)_2Cl_2$ (11 mg, 0.025 mmol, 10 mol%) and copper(I) iodide (10 mg, 0.05 mmol, 20 mol%) in a flame-dried flask. The mixture was degassed with N_2 for 15 min. Phenylacetylene (18 mg, 1.78 mmol) was added, and the mixture was stirred at room temperature overnight. After the completion of reaction, the mixture was diluted with water (3 mL) and then the mixture was extracted with EtOAc (10 mL × 2). The combined organic layers were dried with anhydrous Na_2SO_4, filtered through Celite, and concentrated *in vacuo*. The crude was purified by column chromatography on silica gel (EtOAc in *n*-hexane) to afford 7.

84 mg, 88% yield, pale yellow semi solid, R_f = 0.3 (*n*-hexane:EtOAc = 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.3 Hz, 2H), 7.25 (dtt, *J* = 8.0, 3.0, 1.9 Hz, 11H), 6.81−6.74 (m, 3H), 6.49 (s, 1H), 6.25 (dt, *J* = 10.2, 1.9 Hz, 2H), 6.09 (s, 1H), 5.61 (s, 1H), 3.77 (s, 3H), 3.68 (s, 3H), 2.43 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 184.9, 165.0, 160.1, 148.8, 148.1, 144.0, 141.8, 138.2, 136.9, 131.6, 130.2, 130.1, 129.8, 129.6, 129.4, 128.9, 128.3, 122.0, 121.9, 113.5, 97.1, 82.2, 73.2, 69.2, 55.2, 51.7, 21.5; IR (KBr): 2952, 2839, 2204, 1722, 1667, 1605, 1510, 1337, 1249, 1160, 1067, 909, 729, 667 cm^{-1}; MS (ESI): *m*/*z* 614 (M+Na)$^+$; HRMS (ESI): *m*/*z* calcd for $C_{35}H_{29}NO_6SNa$ (M+Na)$^+$: 614.1608 found: 614.1628.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b01285.

X-ray crystallographic analysis of **4** (CIF)

Copies of ^{1}H and ^{13}C NMR spectra of all new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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