JOC The Journal of Organic Chemistry

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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.8b02188 • Publication Date (Web): 18 Sep 2018

ACS Publications

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Lewis-Base-Catalyzed [1 + 2 + 2] Annulation Reaction of MBH Carbonates with Unsaturated Pyrazolones: Construction of All Stereogenic Carbon Cyclopentane-Fused Dispiropyrazolones

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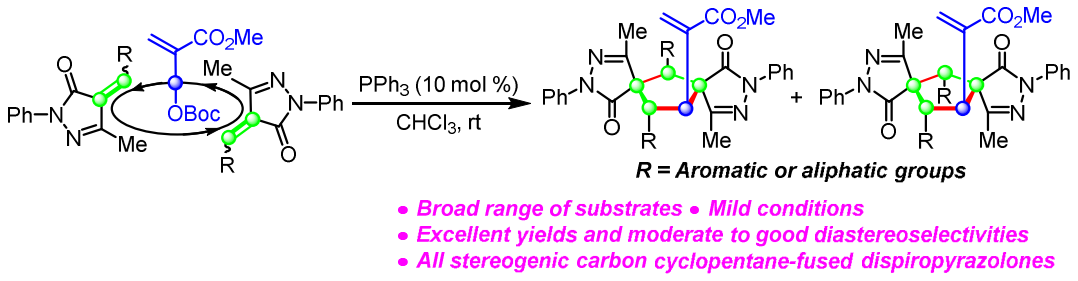


ABSTRACT: The first Lewis-base-catalyzed unexpected [1 + 2 + 2] annulation reaction between MBH carbonates and unsaturated pyrazolones has been developed. The multicyclic cyclopentane-fused dispiropyrazolones constructions containing five contiguous stereogenic centers, including two spiro quaternary centers, were prepared with excellent yields (81%–98%) and moderate to good diastereoselectivies (1:1 to 13: 1). Further transformation and gram-scale operations could also be achieved efficiently.

■ INTRODUCTION

Pyrazolones constitute a privileged class of five-membered aza heterocycles and have attracted considerable attentions because of their wide applications as potential pharmaceutical agents and synthetic scaffolds.[1] For example, pyrazolone derivatives **I**, **II** and **III** (Fig 1) act as neuroprotective agent,[2] HIV integrase inhibitors,[3] and sirtuin inhibitors,[4] respectively. In particular, cyclopentane-related spiropyrazolones, such as **IV**[5] and **V**[6] (Fig 1), have exhibited a promising pharmacophore and many efforts have been invested on their synthesis during the past decades.[7] However, construction of relatively more complicated spiroskeletons, such as the structures introducing two pyrazolone rings into the spirocyclic system, which is called cyclopentane-fused dispiropyrazolones and has all stereogenic centers on cyclopentane (Fig 1, **VI**), is a tough task considering the steric hindrance and stereoselectivity and has not been exploited yet.

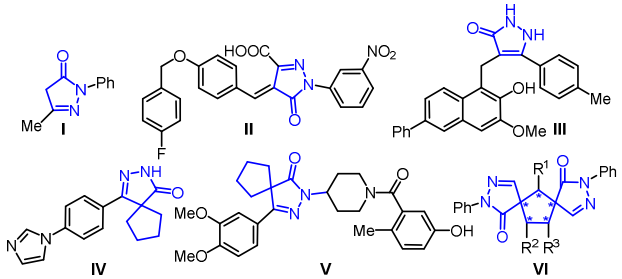


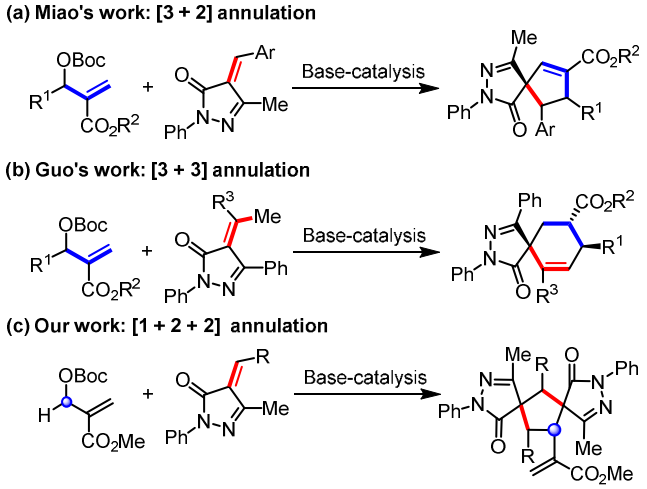
Figure 1. Biologically Active Pyrazolones Motifs.

The convenient, efficient and selective assembly of complex frameworks from simple molecules has always been a challenge yet highly desirable in modern synthetic chemistry. As a form of readily accessible and easy-to-operate powerful building blocks, Morita−Baylis−Hillman (MBH) carbonates have drawn much attention, because of their versatile reaction sites and modes as well as retaining the easily modified double bond in most situations.[8] For instance, as 1,1-dipolar C1 synthons, MBH carbonates have been applied in the construction of five-membered ring compounds with C4 synthons in a [1 + 4] annulation process.[9] They could also be involved in [2 + 4] annulation as a C2 synthons.[10] Moreover, after the pioneering work of Lu's [3 + 2] cycloaddition,[11] MBH carbonates have been used to participate in the reactions as C3 synthons and various annulation reactions such as [3 + 2],[12] [3 + 3],[13] [3 + 4],[14] and [3 + 6][15] patterns, have been developed. Recently, Huang's group has successfully achieved sequential annulation domino reactions using MBH carbonates as 1,2,3-C3 synthons to construct functionalized multicyclic skeletons.[16] Based on the above prominent work, we believe that divergent reaction pathways may occur with MBH carbonates, depending on the structure and nature of the other reaction partners besides catalysts. Therefore, seeking for a suitable nucleophilic or electrophilic partner is the key point to construct divergent fused cyclic architectures.

Unsaturated pyrazolones, functionalized with diverse substituents at *β*-position, exhibit different reactive properties and are ideal candidates to react with MBH carbonates. In 2017, Miao's group[17] disclosed the reactions of aldehyde-derived

MBH carbonates as C3 synthons with α-arylidene pyrazolones in a [3 + 2] manner (Scheme 1a). Recently, Guo's group[18] reported the first Lewis-base-catalyzed enantioselective [3 + 3] annulation reaction of MBH carbonates with β-methyl, aryl double substituted unsaturated pyrazolones (Scheme 1b). Inspired by these prominent developments and as part of our continuing interest in constructing spiropyrazolones,[19] we envisioned the simplest formaldehyde-derived MBH, because of its special zwitterionic intermediates, could lead to a new cyclic process with unsaturated pyrazolones. Herein, we report the realization of a Lewis-base-catalyzed unexpected [1 + 2 + 2] annulation reaction of MBH carbonates with unsaturated pyrazolones, affording biologically and pharmaceutically important cyclopentane-fused dispiropyrazolones bearing a five contiguous stereogenic centers of cyclopentane in excellent yields and with moderate to good diastereoselectivities (Scheme 1c).

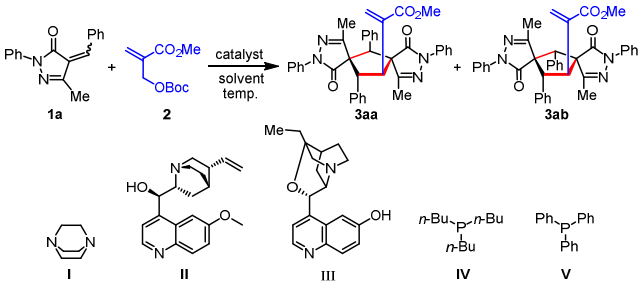
Scheme 1. Annulation of MBH Carbonates with Unsaturated Pyrazolones



■ RESULTS AND DISCUSSION

The initial reaction of unsaturated pyrazolone **1a** (*Z* or *E*) and MBH carbonate **2** proceeded smoothly under the catalysis of PPh_3 (**V**, 10 mol %) in chloroform ($CHCl_3$) at room temperature, delivering the desired spirocyclic product **3a** (two diastereoisomers, major: **3aa** and minor: **3ab**) in 91% yield and with acceptable diastereoselectivity (Table 1, entry 5, dr = 4:1). Trace amount of desired product was obtained while screening a series of amine catalysts and other phosphine catalyst (Table 1, entries 1–4). Subsequently, various polar solvents such as DCM, DCE, THF, acetonitrile, DMF, DMSO and 1,4-dioxone were scanned, and no solvent could improve the diastereoselectivity (Table 1, entries 6–12). Then, protic solvent ethanol (EtOH) was tested and poor yield was obtained because of alcoholysis (Table 1, entry 13). Other solvents such as Et_2O, toluene even hexane were surveyed and no better results were observed (Table 1, entries 15–17). Afterward, further decreasing of the ratio of **1a**/**2** to 1:1.05 finished the reaction in 76% yield and the substrate **1a** could not be consumed thoroughly after 3 h (Table 1, entry 18). High temperature accelerated the reaction and decreased the reaction time to 0.3 h while low temperature prolonged the reaction time (Table 1, entry 19 *vs* entry 20). Accordingly, the best reaction conditions were established as PPh_3 (10 mol %) and **1a**/**2a** (1:1.5) at room temperature or 60 °C in $CHCl_3$.

Table 1. Optimization of the Reaction Conditions[a]



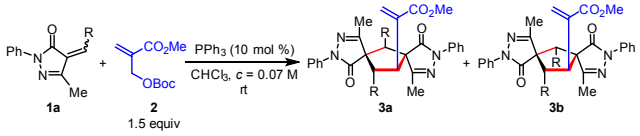
entry	cat.	solvent	t (h)	yield (%)	dr[b] (3aa:3ab)
1	I	$CHCl_3$	48	ND[c]	–
2	II	$CHCl_3$	48	ND	–
3	III	$CHCl_3$	48	ND	–
4	IV	$CHCl_3$	48	trace	–
5	**V**	**$CHCl_3$**	**1**	**91**	**4:1**
6	V	DCM	1	87	2.6:1
7	V	DCE	1	89	2.5:1
8	V	THF	1.5	90	3.5:1
9	V	CH_3CN	1	90	3.3:1
10	V	DMF	1.5	86	2:1
11	V	DMSO	3	83	1.2:1
12	V	1,4-dioxone	48	0	–
13	V	EtOH	1	63	1.4:1
14	V	*i*-PrOH	1	85	1.6:1
15	V	Et_2O	4	88	4:1
16	V	toluene	48	31	–
17	V	hexane	3	90	2.3:1
18[d]	V	$CHCl_3$	3	76	4:1
19[e]	V	$CHCl_3$	0.3	90	4:1
20[f]	V	$CHCl_3$	3	90	4:1

[a]Unless otherwise noted, the reactions were performed on a 0.2 mmol scale of **1a** and **2** (1.5 equiv), using 10 mol % of the catalyst in solvent (3 mL) at rt (22 °C). [b]Determined by ^{1}H NMR. [c]No desired product. [d]The ratio of **1a**/**2** is 1:1.05. [e]The reaction was carried out at 60 °C. [f]The reaction was carried out at 0 °C.

Having established the optimized reaction conditions (Table 1, entry 5 or 19), we set out to investigate the substrate scope of the reaction (Table 2). Generally, in a PPh_3-catalyzed [1 + 2 + 2] process at rt, MBH carbonate **2** could react smoothly with a wide range of aromatic or aliphatic substituted unsaturated pyrazolones **1** to generate the desired products in excellent yields and with moderate to good diastereoselectivities. Unsaturated pyrazolones **1** with electron-withdrawing functional groups, such as halides and nitro substituents in the *ortho*-, *meta*- and *para*-positions exhibited lower diastereoselectivities compared to phenyl group (Table 2, entries 2–7 *vs* entry 1). However, 2-OMe and 4-NMe_2 groups may retain or improve the diastereoselectivity while 3, 4, or 3, 4-electron-donating functional groups still generated unsatisfactory results (Table 2, entries 8 and 12 *vs* entries 9–11). Interestingly, unsaturated pyrazolone substrates **1** bearing 1-naphthyl or 2-naphthyl group (entries 13–14), even heteroaromatic 2-furyl or 2-thienyl group (entries 15–16), were also compatible with the system, furnishing the desired products with excellent yields

and good diastereoselectivities. Moreover, the styryl- or alkyl-substituted unsaturated pyrazolones could also be employed in this annulation but the preferential configuration is **3b** as the major product with reversed diastereoselectivities (entries 17–18). In addition, the structure and stereochemistry of cyclopentane-fused dispiropyrazolone derivatives **3** were determined unambiguously by using single crystal X-ray analysis conducted on the representative product **3ja** and **3db** (Fig 2).[20]

Table 2. Scope of Unsaturated Pyrazolones Derivative 1a[a]



entry	R	3	t (h)	yield[b] (%)	dr[c] (3a:3b)
1	Ph	**3aa/3ab**	1	91	4:1
2	2-ClC_6H_4	**3ba/3bb**	1	82	2.3:1
3	3-ClC_6H_4	**3ca/3cb**	1	88	2.8:1
4	4-ClC_6H_4	**3da/3db**	1	89	2.6:1
5	4-BrC_6H_4	**3ea/3eb**	1	91	2.5:1
6	4-IC_6H_4	**3fa/3fb**	1	83	2.7:1
7	3-$NO_2C_6H_4$	**3ga/3gb**	2	96	1:1
8	2-OMeC_6H_4	**3ha/3hb**	2	94	4:1
9	3-OMeC_6H_4	**3ia/3ib**	2	92	2.4:1
10	4-OMeC_6H_4	**3ja/3jb**	2	88	3.3:1
11	3,4-$(OMe)_2C_6H_3$	**3ka/3kb**	3	98	2.4:1
12	4-$NMe_2C_6H_4$	**3la/3lb**	3.5	94	5:1
13	1-naphthyl	**3ma/3mb**	1	81	12:1
14	2-naphthyl	**3na/3nb**	1	87	5:1
15	2-furyl	**3oa/3ob**	1	92	13:1
16	2-thienyl	**3pa/3pb**	1	95	11.4:1
17	styryl	**3qa/3qb**	1.5	84	1:3.4
18	cyclopropyl	**3ra/3rb**	2	90	1:4.5

[a]The reactions were performed on a 0.2 mmol scale of **1a** and **2** (1.5 equiv), using 10 mol % of PPh_3 in solvent (3 mL) at rt (22 °C). [b]Total yield. [c]Determined by ^1H NMR.

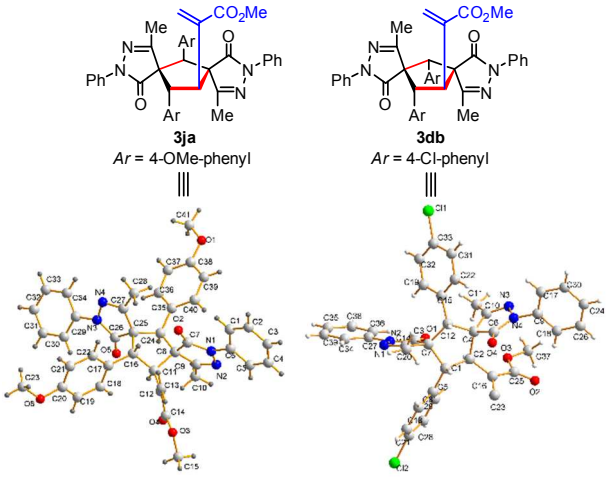
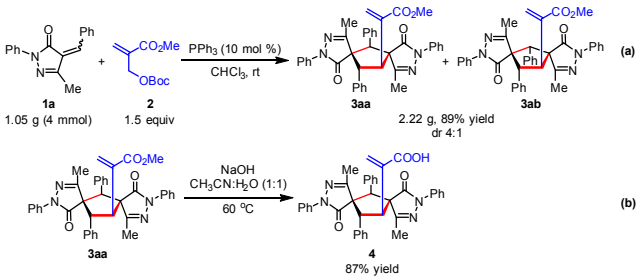


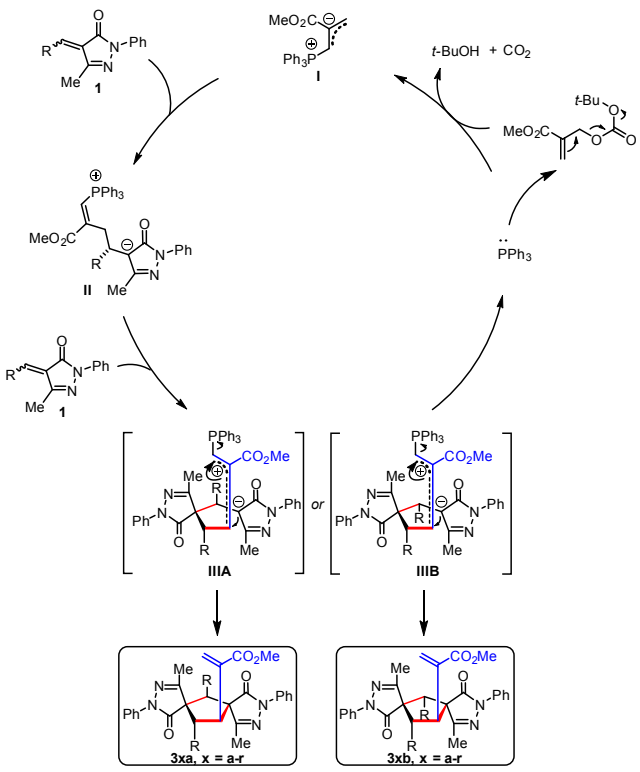
Figure 2. X-ray Structures of 3ja and 3db

To demonstrate the further synthetic utility of this protocol, we carried out the reaction on a gram-scale using **1a** and **2** as the representative substrates to provide **3aa** and **3ab** in total 89% yield (Scheme 2a). The ester group could easily be hydrolyzed, providing the corresponding carboxylic acid **4** with 87% yield (Scheme 2b).

Scheme 2. Gram-scale Synthesis of 3aa/3ab and Further Transformation from 3aa



Scheme 3. Proposed Mechanism



According to the experimental results and previous reports of phosphine-catalyzed annulation reactions,[21] a possible mechanism is proposed to account for the formation of cyclopentane-fused dispiropyrazolone derivatives (Scheme 3). The reaction is initiated by displacement of the carbonate moiety with PPh_3 via an addition-elimination mechanism,[11] which is followed by deprotonation to generate ylide **I**. The nucleophilic attack of **I** to the first molecule of substrate **1** forms intermediate **II**. Subsequently, **II** attacks another molecule of **1**, which is likely proceed in diastereoselective fashion, to give the ylide intermediate **III** in probable two forms. The bulkier aromatic R groups make the intermediate **IIIA** relatively more favorable because of its less steric hindrance between the *anti*-configuration of two aromatic R groups. When R groups are changed to conjugated or aliphatic substitutes, such as styryl and cyclopropyl, respectively, the less bulky R groups make the *syn*-configuration of two R groups possible and intermediate **IIIB** occupies the main configuration instead of intermedi-

ate **IIIA**. It indicates steric hindrance of the R group could change the ratio of preferential conformation.

■ CONCLUSION

In conclusion, we have developed a PPh_3-catalyzed three molecules [1 + 2 + 2] annulation reaction between MBH carbonates and unsaturated pyrazolones for the first time. MBH carbonates serve as 1,1-dipolar C1 synthons to furnish multicyclic cyclopentane-fused dispiropyrazolones with excellent yields and moderate to good diastereoselectivities. In this reaction, A cyclopentane ring with five contiguous stereogenic centers, including two spiro-quaternary centers was formed. Readily available starting materials, inexpensive catalyst, gram-scale synthesis and facile transformation make this reaction valuable in synthetic chemistry. Proposed mechanism is also discussed. Further studies about the asymmetric version of this reaction are underway in our laboratory.

■ EXPERIMENTAL SECTION

General Information. All reactions were performed in oven-dried or flame-dried round-bottom flasks and vials. Stainless steel syringes and cannula were used to transfer air- and moisture-sensitive liquids. Flash chromatography was performed using silica gel 60 (230−400 mesh) from Aladdin. Commercial reagents were purchased from Aladdin, J&K, Macklin and Meryer and used as received. All solvents were used after being freshly distilled unless otherwise noted. Proton nuclear magnetic resonance (^{1}H NMR) spectra and carbon nuclear magnetic resonance ($^{13}C\{^1H\}$ NMR) spectra were recorded on Bruker UltraShield–400 (400 MHz). The mass spectroscopic data were obtained using a Micromass Platform II single quadrupole instrument. Infrared (IR) spectra were obtained using a Perkin Elmer Spectrum 100 FT-IR spectrometer.

General Procedure for the Synthesis of Unsaturated Pyrazolones (1)[19a]**:** Pyrazolone (5.5 mmol, 1.1 equiv) was slowly added to the mixture of the corresponding aldehyde (5 mmol, 1 equiv) and sodium acetate in glacial acetic acid. The mixture was stirred at reflux temperature for 15–60 min. After the reaction was completed, ethyl acetate (50 mL) was added. The precipitate was filtered and the filtrate was washed with water (three times). The combined organic layers were dried over Na_2SO_4 and then concentrated in vacuo. The crude product was obtained after quickly purified by flash column chromatography on silica gel (hexane/EtOAc 5:1). The corresponding products **1** were obtained as red or yellow solid by recrystallization from ethyl acetate.

MBH carbonate (**2**) was prepared through a known procedure.[22]

General Procedure for Lewis-Base-Catalyzed [1 + 2 + 2] Annulation Reaction of MBH Carbonates with Unsaturated Pyrazolones. To a flame-dried sealable 2-dram vial equipped with a stir bar was added unsaturated pyrazolones **1** (0.2 mmol, 1 equiv) and MBH ester **2** (65 mg, 0.3 mmol, 1.5 equiv) under air. Subsequently untreated $CHCl_3$ (3 mL, *c* = 0.07 M) and triphenylphosphine (5.2 mg, 0.02 mmol, 10 mol %) were added to vial via syringe. The reaction mixture was kept stirring for 1–3.5 h at rt (22 °C) until unsaturated pyrazolones **1** was fully consumed (monitored by TLC). Then the organic solvent was removed under reduced pressure and purified through column chromatography (eluent: hexanes and EtOAc) to afford the desired product **3**.

*Methyl 2-((5S,6S,7S,12S,13R)-1,11-dimethyl-4,8-dioxo-3,6,9,13-tetraphenyl-2,3,9,10-tetra azadispiro[4.1.47.25]trideca-1,10-dien-12-yl) acrylate (**3aa**).* The reaction was carried out on a 0.2 mmol scale following the **General Procedure.** The annulation product **3aa** was purified through column chromatography (hexanes/EtOAc: from 8:1 to 6:1) as white solid (**3aa** and **3ab**: 113 mg, dr = 4:1, 91% yield). M. p. 182.7–183.7 °C. IR ν_{max} (neat)/cm^{-1}: 2952, 1720, 1684, 1608, 1510, 1412, 1368, 1293, 1247, 1163, 1022, 923, 758; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, *J* = 5.2 Hz, 2H), 7.48 (t, *J* = 5.2 Hz, 2H), 7.41 (d, *J* = 5.6 Hz, 2H), 7.30–7.27 (m, 3H), 7.23–7.20 (m, 5H), 7.17–7.12 (m, 4H), 6.83 (t, *J* = 2.8 Hz, 2H), 6.27 (s, 1H), 5.78 (s, 1H), 5.09 (d, *J* = 8.8 Hz, 1H), 4.90 (d, *J* = 8.8 Hz, 1H), 4.82 (s, 1H), 3.75 (s, 3H), 2.38 (s, 3H), 2.18 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 175.4, 172.6, 166.7, 161.5, 137.7, 137.3, 134.7, 133.2, 132.9, 129.6, 129.2, 129.0, 128.6, 128.4, 128.2, 128.0, 127.8, 126.5, 125.7, 125.3, 119.8, 119.5, 67.7, 65.9, 54.8, 52.2, 50.9, 46.0, 16.0, 13.9. HRMS (ESI, m/z): calcd for $C_{39}H_{35}N_4O_4^+$, $[M + H]^+$, 623.2653, found 623.2653.

*Methyl 2-((5S,6S,7S,12S,13S)-6,13-bis(2-chlorophenyl)-1,11-dimethyl-4,8-dioxo-3,9-diphenyl-2,3,9, 10-tetraazadispiro[4.1.47.25]trideca-1,10-dien-12-yl)acrylate (**3ba**).* The reaction was carried out on a 0.2 mmol scale following the **General Procedure**. The annulation product **3ba** and **3bb** were purified through column chromatography (hexanes/EtOAc: from 8:1 to 6:1) as white solid (total **3b**: 114 mg, dr = 2.3:1, 82% yield). M. p. 181.3–182.2 °C. IR ν_{max} (neat)/cm^{-1}: 2989, 2932, 1725, 1712, 1607, 1499, 1368, 1314, 1247, 1013, 925, 738; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, *J* = 5.2 Hz, 2H), 7.48–7.45 (m, 4H), 7.34–7.28 (m, 3H), 7.20–7.16 (m, 5H), 7.10 (d, *J* = 5.2 Hz, 2H), 6.79 (d, *J* = 5.6 Hz, 2H), 6.28 (s, 1H), 5.76 (s, 1H), 5.06 (d, *J* = 8.8 Hz, 1H), 4.83 (d, *J* = 8.8 Hz, 1H), 4.73 (s, 1H), 3.75 (s, 3H), 2.36 (s, 3H), 2.22 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 175.1, 172.3, 166.6, 161.0, 137.6, 137.1, 134.2, 134.1, 133.0, 132.8, 131.8, 129.6, 129.4, 129.0, 128.7, 128.7, 128.1, 125.9, 125.6, 119.8, 119.4, 67.4, 66.0, 54.5, 52.3, 50.3, 46.1, 16.1, 13.8. HRMS (ESI, m/z): calcd for $C_{39}H_{33}Cl_2N_4O_4^+$, $[M + H]^+$, 691.1873, found 691.1872.

*Methyl 2-((5S,6R,7S,12S,13S)-6,13-bis(2-chlorophenyl)-1,11-dimethyl-4,8-dioxo-3,9-diphenyl-2,3,9, 10-tetraazadispiro[4.1.47.25]trideca-1,10-dien-12-yl)acrylate (**3bb**).* M. p. 183.5–184.6 °C. IR ν_{max} (neat)/cm^{-1}: 2957, 1716, 1707, 1628, 1513, 1402, 1339, 1189, 1054, 931, 767; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, *J* = 5.2 Hz, 2H), 7.50 (t, *J* = 5.2 Hz, 2H), 7.44 (t, *J* = 5.6 Hz, 2H), 7.38 (d, *J* = 5.6 Hz, 2H), 7.28–7.21 (m, 4H), 7.18 (d, *J* = 5.6 Hz, 2H), 7.14 (d, *J* = 5.6 Hz, 2H), 6.76 (d, *J* = 5.6 Hz, 2H), 6.29 (s, 1H), 5.67 (s, 1H), 5.51 (d, *J* = 8.8 Hz, 1H), 4.62 (s, 1H), 4.23 (d, *J* = 8.8 Hz, 1H), 3.65 (s, 3H), 2.37 (s, 3H), 2.19 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 175.2, 172.1, 166.4, 163.0, 159.1, 137.6, 137.1, 134.5, 134.1, 133.7, 132.8, 130.7, 129.7, 129.4, 129.3, 128.9, 128.0, 126.0, 125.5, 119.9, 119.3, 66.6, 66.1, 54.8, 52.9, 52.0, 44.8, 16.5, 13.5. HRMS (ESI, m/z): calcd for $C_{39}H_{33}Cl_2N_4O_4^+$, $[M + H]^+$, 691.1873, found 691.1871.

*Methyl 2-((5S,6S,7S,12S,13R)-6,13-bis(3-chlorophenyl)-1,11-dimethyl-4,8-dioxo-3,9-diphenyl-2,3,9, 10-tetraazadispiro[4.1.47.25]trideca-1,10-dien-12-yl)acrylate (**3ca**).* The reaction was carried out on a 0.2 mmol scale following the **General Procedure**. The annulation product **3ca** and **3cb** were purified through column chromatography (hexanes/EtOAc: from 8:1 to 6:1) as white solid (total **3c**: 121 mg,

dr = 2.8:1, 88% yield). M. p. 184.3–185.3 °C. IR ν_{max} (neat)/cm^{-1}: 2980, 2923, 1731, 1712, 1629, 1608, 1511, 1375, 1304, 1250, 941, 775; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 0.4 Hz, 2H), 7.49–7.45 (m, 4H), 7.34–7.30 (m, 3H), 7.22 (d, *J* = 5.6 Hz, 1H), 7.18–7.14 (m, 5H), 7.06 (d, *J* = 4.8 Hz, 1H), 6.83 (s, 1H), 6.72 (d, *J* = 5.6 Hz, 1H), 6.30 (s, 1H), 5.78 (s, 1H), 5.04 (d, *J* = 8.8 Hz, 1H), 4.82 (d, *J* = 8.8 Hz, 1H), 4.74 (s, 1H), 3.76 (s, 3H), 2.37 (s, 3H), 2.20 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 174.9, 172.2, 166.5, 161.0, 160.8, 137.4, 137.1, 136.5, 135.2, 135.2, 134.4, 132.6, 130.4, 129.7, 129.0, 128.7, 128.4, 128.4, 128.2, 127.0, 126.4, 126.1, 125.6, 124.7, 120.1, 119.5, 67.3, 65.7, 54.2, 52.3, 50.4, 45.9, 16.1, 13.8. HRMS (ESI, m/z): calcd for $C_{39}H_{33}Cl_2N_4O_4^+$, $[M + H]^+$, 691.1873, found 691.1873.

*Methyl 2-((5S,6R,7S,12S,13R)-6,13-bis(3-chlorophenyl)-1,11-dimethyl-4,8-dioxo-3,9-diphenyl-2,3,9, 10-tetraazadispiro[4.1.47.25]trideca-1,10-dien-12-yl)acrylate **(3cb)**.* M. p. 181.1–182.1 °C. IR ν_{max} (neat)/cm^{-1}: 2966, 1721, 1716, 1618, 1611, 1524, 1366, 1312, 1197, 920, 744; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, *J* = 5.2 Hz, 2H), 7.50 (d, *J* = 5.2 Hz, 2H), 7.45 (t, *J* = 5.2 Hz, 2H), 7.38 (t, *J* = 5.2 Hz, 2H), 7.26–7.12 (m, 8H), 6.81 (s, 1H), 6.71 (d, *J* = 5.2 Hz, 1H), 6.32 (s, 1H), 5.70 (s, 1H), 5.51 (d, *J* = 8.8 Hz, 1H), 4.62 (s, 1H), 4.22 (d, *J* = 8.8 Hz, 1H), 3.66 (s, 3H), 2.38 (s, 3H), 2.19 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 175.1, 172.0, 166.3, 162.9, 158.9, 137.6, 137.0, 136.3, 135.2, 134.7, 134.3, 133.7, 130.4, 129.9, 129.7, 128.9, 128.9, 128.2, 128.2, 127.0, 126.2, 125.6, 124.8, 120.3, 119.5, 66.3, 65.9, 54.6, 53.0, 52.0, 44.7, 16.4, 13.5. HRMS (ESI, m/z): calcd for $C_{39}H_{33}Cl_2N_4O_4^+$, $[M + H]^+$, 691.1873, found 691.1873.

*Methyl 2-((5S,6S,7S,12S,13R)-6,13-bis(4-chlorophenyl)-1,11-dimethyl-4,8-dioxo-3,9-diphenyl-2,3,9, 10-tetraazadispiro[4.1.47.25]trideca-1,10-dien-12-yl)acrylate **(3da)**.* The reaction was carried out on a 0.2 mmol scale following the **General Procedure**. The annulation product **3da** and **3db** were purified through column chromatography (hexanes/EtOAc: from 8:1 to 6:1) as white solid (total **3d**: 123 mg, dr = 2.6:1, 89% yield). M. p. 185.6–186.6 °C. IR ν_{max} (neat)/cm^{-1}: 2985, 2967, 1709, 1705, 1625, 1604, 1508, 1486, 1412, 1377, 1252, 1163, 1011, 910, 728; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 5.6 Hz, 2H), 7.49–7.45 (m, 4H), 7.34–7.28 (m, 3H), 7.22–7.14 (m, 6H), 7.07 (d, *J* = 4.4 Hz, 1H), 6.83 (s, 1H), 6.72 (d, *J* =4.8 Hz, 1H), 6.30 (s, 1H), 5.78 (s, 1H), 5.04 (d, *J* = 8.8 Hz, 1H), 4.82 (d, *J* = 8.8 Hz, 1H), 4.74 (s, 1H), 3.77 (s, 3H), 2.38 (s, 3H), 2.20 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 174.9, 172.2, 166.5, 161.0, 160.8, 137.4, 137.1, 136.5, 135.2, 134.4, 132.6, 130.4, 129.7, 129.0, 128.7, 128.4, 128.3, 128.2, 127.0, 126.4, 126.1, 125.6, 124.7, 120.1, 119.5, 67.3, 65.7, 54.2, 52.3, 50.4, 45.9, 16.1, 13.8. HRMS (ESI, m/z): calcd for $C_{39}H_{33}Cl_2N_4O_4^+$, $[M + H]^+$, 691.1873, found 691.1875.

*Methyl 2-((5S,6R,7S,12S,13R)-6,13-bis(4-chlorophenyl)-1,11-dimethyl-4,8-dioxo-3,9-diphenyl-2,3,9, 10-tetraazadispiro[4.1.47.25]trideca-1,10-dien-12-yl)acrylate **(3db)**.* M. p. 184.8–185.8 °C. IR ν_{max} (neat)/cm^{-1}: 2977, 1722, 1706, 1611, 1548, 1435, 1403, 1369, 1224, 1106, 1015, 932, 743; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, *J* = 5.2 Hz, 2H), 7.50 (d, *J* = 5.2 Hz, 2H), 7.44 (t, *J* = 5.6 Hz, 2H), 7.38 (t, *J* = 5.2 Hz, 2H), 7.28–7.14 (m, 8H), 6.76 (d, *J* = 5.2 Hz, 2H), 6.29 (s, 1H), 5.67 (s, 1H), 5.51 (d, *J* = 8.8 Hz, 1H), 4.62 (s, 1H), 4.23 (d, *J* = 8.8 Hz, 1H), 3.65 (s, 3H), 2.36 (s, 3H), 2.19 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 175.1, 171.9, 166.3, 162.9, 159.0, 137.0, 136.3, 135.2, 134.7, 134.3, 133.6, 130.4, 129.9, 129.7, 128.9, 128.9, 128.8, 128.2, 128.1, 127.0, 126.1, 125.7, 124.7, 120.3, 119.5, 66.3, 65.9, 54.6, 53.0, 52.0, 44.6, 16.4, 13.5. HRMS (ESI, m/z): calcd for $C_{39}H_{33}Cl_2N_4O_4^+$, $[M + H]^+$, 691.1873, found 691.1873.

*Methyl 2-((5S,6S,7S,12S,13R)-6,13-bis(4-bromophenyl)-1,11-dimethyl-4,8-dioxo-3,9-diphenyl-2,3,9,10-tetraazadispiro[4.1.47.25]trideca-1,10-dien-12-yl)acrylate **(3ea)**.* The reaction was carried out on a 0.2 mmol scale following the **General Procedure**. The annulation product **3ea** and **3eb** were purified through column chromatography (hexanes/EtOAc: from 8:1 to 6:1) as white solid (total **3e**: 142 mg, dr = 2.5:1, 91% yield). M. p. 191.5–192.5 °C. IR ν_{max} (neat)/cm^{-1}: 2986, 2942, 1720, 1598, 1513, 1501, 1479, 1242, 1147, 1090, 1017, 913, 740; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, *J* = 5.2 Hz, 2H), 7.47 (t, *J* = 4.8 Hz, 2H), 7.44 (d, *J* = 5.2 Hz, 2H), 7.35–7.28 (m, 7H), 7.18 (t, *J* = 4.8 Hz, 1H), 7.04 (d, *J* = 6.0 Hz, 2H), 6.71 (d, *J* = 5.6 Hz, 2H), 6.28 (s, 1H), 5.76 (s, 1H), 5.04 (d, *J* = 8.8 Hz, 1H), 4.82 (d, *J* = 8.8 Hz, 1H), 4.70 (s, 1H), 3.75 (s, 3H), 2.36 (s, 3H), 2.20 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 175.0, 172.2, 166.5, 161.0, 161.0, 137.4, 137.0, 133.5, 132.6, 132.4, 132.2, 131.6, 129.9, 129.7, 129.0, 128.7, 128.3, 125.9, 125.6, 122.3, 122.0, 119.7, 119.4, 67.2, 65.8, 54.4, 52.3, 50.3, 46.0, 16.1, 13.8. HRMS (ESI, m/z): calcd for $C_{39}H_{33}Br_2N_4O_4^+$, $[M + H]^+$, 779.0863, found 779.0865.

*Methyl 2-((5S,6R,7S,12S,13R)-6,13-bis(4-bromophenyl)-1,11-dimethyl-4,8-dioxo-3,9-diphenyl-2,3,9,10-tetraazadispiro[4.1.47.25]trideca-1,10-dien-12-yl)acrylate **(3eb)**.* M. p. 193.1–194.1 °C. IR ν_{max} (neat)/cm^{-1}: 2955, 2820, 1713, 1608, 1522, 1484, 1233, 1099, 1016, 936, 755; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, *J* = 5.2 Hz, 2H), 7.49 (d, *J* = 5.2 Hz, 2H), 7.44 (t, *J* = 5.2 Hz, 2H), 7.40–7.33 (m, 6H), 7.25–7.23 (m, 2H), 7.08 (d, *J* = 5.6 Hz, 2H), 6.71 (d, *J* = 5.6 Hz, 2H), 6.29 (s, 1H), 5.67 (s, 1H), 5.50 (d, *J* = 8.8 Hz, 1H), 4.60 (s, 1H), 4.22 (d, *J* = 8.8 Hz, 1H), 3.65 (s, 3H), 2.36 (s, 3H), 2.19 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 175.1, 172.0, 166.4, 163.0, 159.1, 137.6, 137.0, 133.6, 133.3, 132.4, 131.9, 131.2, 129.7, 129.6, 128.9, 128.3, 126.1, 125.5, 122.7, 122.1, 119.9, 119.3, 66.5, 66.0, 54.8, 52.9, 52.0, 44.7, 16.5, 13.5. HRMS (ESI, m/z): calcd for $C_{39}H_{33}Br_2N_4O_4^+$, $[M + H]^+$, 779.0863, found 779.0865.

*Methyl 2-((5S,6S,7S,12S,13R)-6,13-bis(4-iodophenyl)-1,11-dimethyl-4,8-dioxo-3,9-diphenyl-2,3,9,10-tetraazadispiro[4.1.47.25]trideca-1,10-dien-12-yl)acrylate **(3fa)**.* The reaction was carried out on a 0.2 mmol scale following the **General Procedure**. The annulation product **3fa** and **3fb** were purified through column chromatography (hexanes/EtOAc: from 8:1 to 6:1) as white solid (total **3f**: 149mg, dr = 2.7:1, 83% yield). M. p. 197.5–198.5 °C. IR ν_{max} (neat)/cm^{-1}: 2976, 2933, 1715, 1709, 1641, 1597, 1506, 1372, 1288, 1241, 922, 730; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, *J* = 5.2 Hz, 2H), 7.55–7.53 (m, 4H), 7.48–7.45 (m, 2H), 7.40 (dd, *J* = 0.8, 2.0 Hz, 2H), 7.35–7.32 (m, 2H), 7.29–7.28 (m, 1H), 7.19 (t, *J* = 5.2 Hz, 1H), 6.90 (d, *J* = 5.6 Hz, 2H), 6.57 (d, *J* = 5.6 Hz, 2H), 6.27 (s, 1H), 5.75 (s, 1H), 5.01 (d, *J* = 8.8 Hz, 1H), 4.80 (d, *J* = 8.8 Hz, 1H), 4.68 (s, 1H), 3.74 (s, 3H), 2.35 (s, 3H), 2.19 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 175.0, 172.2, 166.5, 161.1, 161.0, 138.3, 137.6, 137.5, 137.0, 134.2, 132.9, 130.1, 129.7, 129.0, 128.8, 128.5, 125.9, 125.7, 119.7, 119.5, 93.8, 93.4, 67.2, 65.8, 54.5, 52.3, 50.4, 45.8, 16.1, 13.8. HRMS (ESI, m/z): calcd for $C_{39}H_{32}I_2N_4O_4Na^+$, $[M + H]^+$, 897.0405, found 897.0406.

*Methyl 2-((5S,6R,7S,12S,13R)-6,13-bis(4-iodophenyl)-1,11-dimethyl-4,8-dioxo-3,9-diphenyl -2,3,9,10-tetraazadispiro[4.1.47.25]trideca-1,10-dien-12-yl)acrylate **(3fb)**.* M. p.

194.5–195.5 °C. IR ν_{max} (neat)/cm^{-1}: 2991, 2879, 1722, 1702, 1655, 1571, 1489, 1344, 1267, 1183, 1070, 941, 752; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, *J* = 5.2 Hz, 2H), 7.56 (d, *J* = 5.2 Hz, 4H), 7.53 (d, *J* = 5.2 Hz, 2H), 7.48 (d, *J* = 5.6 Hz, 2H), 7.44 (t, *J* = 5.2 Hz, 2H), 7.39 (t, *J* = 5.2 Hz, 2H), 7.25–7.24 (m, 2H), 6.94 (d, *J* = 5.6 Hz, 2H), 6.56 (d, *J* = 5.6 Hz, 2H), 6.29 (s, 1H), 5.67 (s, 1H), 5.49 (d, *J* = 8.8 Hz, 1H), 4.58 (s, 1H), 4.19 (d, *J* = 8.8 Hz, 1H), 3.64 (s, 3H), 2.35 (s, 3H), 2.18 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 175.1, 172.0, 166.4, 163.0, 159.0, 138.3, 137.8, 137.6, 137.0, 134.0, 131.9, 129.8, 128.9, 128.5, 126.1, 125.5, 120.0, 119.3, 94.3, 93.5, 66.4, 66.0, 54.9, 53.0, 52.0, 44.6, 16.5, 13.5. HRMS (ESI, m/z): calcd for $C_{39}H_{32}I_2N_4O_4Na^+$, $[M + H]^+$, 897.0405, found 897.0404.

*Methyl 2-((5S,6S,7S,12S,13R)-1,11-dimethyl-6,13-bis(3-nitrophenyl)-4,8-dioxo-3,9-diphenyl -2,3,9,10-tetraazadispiro [4.1.47.25]trideca-1,10-dien-12-yl)acrylate (**3ga**).* The reaction was carried out on a 0.2 mmol scale following the **General Procedure**. The annulation product **3ga** and **3gb** were purified through column chromatography (hexanes/EtOAc: from 6:1 to 4:1) as white solid (total **3g**: 137 mg, dr 1:1, 96% yield). M. p. 178.5–179.5 °C. IR ν_{max} (neat)/cm^{-1}: 2981, 2962, 2938, 1736, 1711, 1704, 1595, 1530, 1487, 1386, 1355, 1249, 1152, 931, 763; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (d, *J* = 5.2 Hz, 1H), 8.04 (s, 1H), 8.03 (d, *J* = 5.6 Hz, 1H), 7.83 (d, *J* = 5.2 Hz, 2H), 7.82 (s, 1H), 7.55–7.42 (m, 7H), 7.34–7.28 (m, 3H), 7.17 (t, *J* = 4.8 Hz, 1H), 7.11 (d, *J* = 4.8 Hz, 1H), 6.34 (s, 1H), 5.84 (s, 1H), 5.21 (d, *J* = 8.8 Hz, 1H), 4.96 (d, *J* = 8.8 Hz, 1H), 4.85 (s, 1H), 3.79 (s, 3H), 2.41 (s, 3H), 2.21 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 174.5, 171.9, 166.3, 160.4, 160.3, 148.7, 148.3, 137.1, 136.8, 136.5, 135.3, 134.1, 132.7, 132.4, 130.4, 130.0, 129.6, 128.8, 126.4, 125.9, 123.3, 123.1, 121.5, 120.3, 119.1, 67.1, 65.6, 54.2, 52.6, 50.3, 45.9, 16.2, 13.8. HRMS (ESI, m/z): calcd for $C_{39}H_{33}N_6O_8^+$, $[M + H]^+$, 713.2354, found 713.2358.

*Methyl 2-((5S,6R,7S,12S,13R)-1,11-dimethyl-6,13-bis(3-nitrophenyl)-4,8-dioxo-3,9-diphenyl-2,3,9,10-tetraazadispiro [4. 1.47.25]trideca-1,10-dien-12-yl)acrylate (**3gb**).* M. p. 181.5–182.5 °C. IR ν_{max} (neat)/cm^{-1}: 2973, 2895, 1722, 1714, 1697, 1568, 1492, 1377, 1320, 1232, 1149, 957, 733; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13–8.09 (m, 3H), 7.83 (d, *J* = 4.8 Hz, 2H), 7.77 (s, 1H), 7.61 (d, *J* = 4.8 Hz, 1H), 7.52 (d, *J* = 5.6 Hz, 2H), 7.48–7.43 (m, 4H), 7.37 (t, *J* = 5.2 Hz, 2H), 7.28 (t, *J* = 5.2 Hz, 1H), 7.23 (t, *J* = 5.2 Hz, 1H), 7.12 (d, *J* = 5.2 Hz, 1H), 6.34 (s, 1H), 5.76 (s, 1H), 5.63 (d, *J* = 8.8 Hz, 1H), 4.77 (s, 1H), 4.42 (d, *J* = 8.8 Hz, 1H), 3.68 (s, 3H), 2.45 (s, 3H), 2.17 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 174.8, 171.5, 166.2, 162.2, 158.5, 148.7, 148.4, 137.4, 136.3, 134.3, 133.6, 132.6, 130.4, 130.1, 129.9, 129.0, 129.0, 126.4, 126.0, 123.7, 123.3, 123.1, 121.6, 120.0, 119.6, 66.3, 65.8, 54.4, 52.9, 52.2, 44.6, 16.4, 13.5. HRMS (ESI, m/z): calcd for $C_{39}H_{33}N_6O_8^+$, $[M + H]^+$, 713.2354, found 713.2357.

*Methyl 2-((5S,7S,12R)-6,13-bis(2-methoxyphenyl)-1,11-dimethyl-4,8-dioxo-3,9-diphenyl-2,3,9,10-tetraazadispiro[4.1. 47.25]trideca-1,10-dien-12-yl)acrylate (**3ha**).* The reaction was carried out on a 0.2 mmol scale following the **General Procedure**. The annulation product **3ha** was purified through column chromatography (hexanes/EtOAc: from 6:1 to 4:1) as white solid (total **3h**: 132 mg, dr = 4:1, 94% yield). M. p. 193.2–194.2 °C. IR ν_{max} (neat)/cm^{-1}: 3081, 3033, 2975, 2932, 2847, 1726, 1219, 1696, 1634, 1593, 1489, 1377, 1292, 1256, 1121, 1025, 775; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, *J* = 4.8 Hz, 2H), 7.51–7.46 (m, 3H), 7.32 (d, *J* = 4.4 Hz, 1H), 7.27 (t, *J* = 5.2 Hz, 1H), 7.23–7.21 (m, 4H), 7.08–7.04 (m, 2H), 6.93 (d, *J* = 5.2 Hz, 1H), 6.84 (dd, *J* = 0.8, 5.2 Hz, 1H), 6.79 (dd, *J* = 0.8, 5.2 Hz, 1H), 6.73 (d, *J* = 5.2 Hz, 1H), 6.67 (d, *J* = 4.8 Hz, 1H), 6.20 (s, 1H), 5.68 (d, *J* = 8.8 Hz, 1H), 5.67 (s, 1H), 4.88 (d, *J* = 8.8 Hz, 1H), 4.79 (s, 1H), 3.74 (s, 3H), 3.73 (s, 3H), 3.36 (s, 3H), 2.34 (s, 3H), 1.91 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 176.1, 173.0, 166.8, 161.7, 158.1, 156.9, 138.0, 137.8, 133.0, 129.5, 128.9, 128.8, 128.5, 128.3, 126.6, 125.5, 124.1, 123.4, 122.1, 120.5, 120.3, 119.9, 118.4, 109.8, 109.7, 65.4, 55.0, 54.5, 52.0, 49.7, 46.0, 42.7, 15.7, 14.1, 14.0. HRMS (ESI, m/z): calcd for $C_{41}H_{38}N_4O_6Na^+$, $[M + H]^+$, 705.2684, found 705.2684.

*Methyl 2-((5S,6S,7S,12S,13R)-6,13-bis(3-methoxyphenyl)-1,11-dimethyl-4,8-dioxo-3,9-diphenyl-2,3,9,10-tetraazadispiro [4.1.47.25]trideca-1,10-dien-12-yl)acrylate (**3ia**).* The reaction was carried out on a 0.2 mmol scale following the **General Procedure**. The annulation product **3ia** and **3ib** were purified through column chromatography (hexanes/EtOAc: from 6:1 to 4:1) as white solid (total **3i**: 126 mg, dr = 2.4:1, 92% yield). M. p. 184.7–185.7 °C. IR ν_{max} (neat)/cm^{-1}: 2947, 2838, 1711, 1596, 1584, 1502, 1433, 1410, 1382, 1298, 1233, 1155, 1049, 922, 774; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, *J* = 5.2 Hz, 2H), 7.48–7.45 (m, 4H), 7.31–7.26 (m, 3H), 7.15–7.09 (m, 3H), 6.77–6.73 (m, 3H), 6.68 (dd, *J* = 1.2, 5.2 Hz, 1H), 6.40 (d, *J* = 5.2 Hz, 1H), 6.36 (s, 1H), 6.28 (s, 1H), 5.81 (s, 1H), 5.05 (d, *J* = 8.8 Hz, 1H), 4.85 (d, *J* = 8.8 Hz, 1H), 4.79 (s, 1H), 3.75 (s, 3H), 3.72 (s, 3H), 3.54 (s, 3H), 2.39 (s, 3H), 2.20 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 175.4, 172.6, 166.7, 161.6, 161.5, 160.0, 159.5, 137.7, 137.4, 136.1, 134.7, 130.1, 129.5, 129.3, 128.9, 128.6, 125.7, 125.2, 120.6, 119.7, 119.3, 118.6, 114.0, 113.9, 113.7, 111.5, 67.5, 65.9, 55.2, 54.9, 52.2, 50.9, 46.0, 16.1, 13.8. HRMS (ESI, m/z): calcd for $C_{41}H_{39}N_4O_6^+$, $[M + H]^+$, 683.2864, found 683.2861.

*Methyl 2-((5S,6R,7S,12S,13R)-6,13-bis(3-methoxyphenyl)-1,11-dimethyl-4,8-dioxo-3,9-diphenyl-2,3,9,10-tetraazadispiro [4.1.47.25]trideca-1,10-dien-12-yl)acrylate (**3ib**).* M. p. 187.9–188.9 °C. IR ν_{max} (neat)/cm^{-1}: 2962, 2873, 1715, 1622, 1546, 1498, 1403, 1355, 1288, 1210, 1134, 1017, 944, 758; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, *J* = 5.2 Hz, 2H), 7.56 (d, *J* = 5.2 Hz, 2H), 7.43 (t, *J* = 5.2 Hz, 2H), 7.35 (t, *J* = 5.2 Hz, 2H), 7.24 (t, *J* = 4.8 Hz, 1H), 7.19 (t, *J* = 4.8 Hz, 1H), 7.15 (t, *J* = 5.2 Hz, 1H), 7.09 (t, *J* = 5.2 Hz, 1H), 6.81 (d, *J* = 5.2 Hz, 1H), 6.76 (s, 1H), 6.75–6.71 (m, 2H), 6.39 (d, *J* = 5.2 Hz, 1H), 6.35 (s, 1H), 6.30 (s, 1H), 5.73 (s, 1H), 5.53 (d, *J* = 8.8 Hz, 1H), 4.66 (s, 1H), 4.22 (d, *J* = 8.8 Hz, 1H), 3.69 (s, 3H), 3.65 (s, 3H), 3.52 (s, 3H), 2.38 (s, 3H), 2.20 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 175.5, 172.5, 166.5, 163.7, 160.0, 159.7, 137.8, 137.4, 135.9, 133.8, 130.1, 129.5, 128.8, 128.7, 125.6, 125.4, 120.4, 119.9, 119.3, 118.7, 114.2, 113.9, 113.8, 111.6, 66.5, 66.2, 55.3, 55.2, 54.9, 53.6, 51.9, 44.7, 16.5, 13.5. HRMS (ESI, m/z): calcd for $C_{41}H_{39}N_4O_6^+$, $[M + H]^+$, 683.2864, found 683.2862.

*Methyl 2-((5S,6S,7S,12S,13R)-6,13-bis(4-methoxyphenyl)-1,11-dimethyl-4,8-dioxo-3,9-diphenyl-2,3,9,10-tetraazadispiro [4.1.47.25]trideca-1,10-dien-12-yl)acrylate (**3ja**).* The reaction was carried out on a 0.2 mmol scale following the **General Procedure**. The annulation product **3ja** and **3jb** were purified through column chromatography (hexanes/EtOAc: from 6:1 to 4:1) as white solid (total **3j**: 120 mg, dr = 3.3:1, 88% yield). M. p. 185.4–186.5 °C. IR ν_{max} (neat)/cm^{-1}: 3175, 3008, 2920, 2887, 1712, 1609, 1593, 1534, 1498, 1375, 1290, 1231, 940, 914, 852; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, *J* = 5.2 Hz, 2H), 7.47 (t, *J* = 5.2 Hz, 4H), 7.31–7.28 (m, 3H), 7.13 (t, *J* =

4.8 Hz, 1H), 7.10 (t, *J* = 10.0 Hz, 2H), 6.78 (d, *J* = 6.0 Hz, 2H), 6.73 (dd, *J* = 5.6, 8.4 Hz, 4H), 6.27 (s, 1H), 5.77 (s, 1H), 5.05 (d, *J* = 8.8 Hz, 1H), 4.82 (d, *J* = 8.8 Hz, 1H), 4.74 (s, 1H), 3.74 (s, 3H), 3.73 (s, 3H), 3.67 (s, 3H), 2.37 (s, 3H), 2.22 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 175.6, 172.6, 166.7, 161.7, 161.6, 159.3, 159.0, 137.7, 137.4, 133.0, 129.5, 129.3, 128.9, 128.5, 127.8, 126.5, 125.7, 125.3, 125.2, 119.8, 119.4, 114.5, 113.9, 67.7, 66.2, 55.1, 54.5, 52.1, 50.4, 46.2, 16.1, 13.8. HRMS (ESI, m/z): calcd for $C_{41}H_{39}N_4O_6^+$, $[M + H]^+$, 683.2864, found 683.2864.

Methyl 2-((5S,6R,7S,12S,13R)-6,13-bis(4-methoxyphenyl)-1,11-dimethyl-4,8-dioxo-3,9-diphenyl-2,3,9,10-tetraazadispiro[4.1.47.25]trideca-1,10-dien-12-yl)acrylate ***(3jb)***. M. p. 192.5–193.5 °C. IR ν_{max} (neat)/cm^{-1}: 3083, 2911, 2865, 1721, 1624, 1576, 1482, 1367, 1283, 1179, 922, 745; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, *J* = 5.2 Hz, 2H), 7.53 (d, *J* = 5.2 Hz, 2H), 7.43 (t, *J* = 5.2 Hz, 2H), 7.36 (d, *J* = 5.2 Hz, 2H), 7.24–7.20 (m, 2H), 7.13 (d, *J* = 5.6 Hz, 2H), 6.77 (d, *J* = 6.0 Hz, 2H), 6.75 (d, *J* = 6.0 Hz, 2H), 6.71 (d, *J* = 6.0 Hz, 2H), 6.28 (s, 1H), 5.68 (s, 1H), 5.51 (d, *J* = 8.8 Hz, 1H), 4.61 (s, 1H), 4.22 (d, *J* = 8.8 Hz, 1H), 3.73 (s, 3H), 3.70 (s, 3H), 3.64 (s, 3H), 2.36 (s, 3H), 2.21 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 175.6, 172.7, 166.6, 159.7, 159.2, 137.5, 134.1, 129.5, 129.1, 128.8, 128.8, 127.9, 126.3, 125.7, 125.3, 120.1, 119.3, 114.5, 114.1, 67.1, 66.3, 55.2, 55.0, 53.1, 51.9, 45.0, 16.5, 13.5. HRMS (ESI, m/z): calcd for $C_{41}H_{39}N_4O_6^+$, $[M + H]^+$, 683.2864, found 683.2867.

Methyl 2-((5S,6S,7S,12S,13R)-6,13-bis(3,4-dimethoxyphenyl)-1,11-dimethyl-4,8-dioxo-3,9-diphenyl-2,3,9,10-tetra-azadispiro[4.1.47.25]trideca-1,10-dien-12-yl)acrylate ***(3ka)***. The reaction was carried out on a 0.2 mmol scale following the **General Procedure**. The annulation product **3ka** and **3kb** were purified through column chromatography (hexanes/EtOAc: from 5:1 to 3:1) as white solid (total **3k**: 150 mg, dr = 2.4:1, 98% yield). M. p. 178.5–179.5 °C. IR ν_{max} (neat)/cm^{-1}: 2980, 1725, 1712, 1704, 1641, 1609, 1518, 1497, 1411, 1392, 1265, 1167, 920, 775; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, *J* = 5.2 Hz, 2H), 7.50 (dd, *J* = 0.8, 6.0 Hz, 2H), 7.46 (t, *J* = 5.6 Hz, 2H), 7.31–7.28 (m, 2H), 7.26 (t, *J* = 5.2 Hz, 1H), 7.13 (t, *J* = 5.2 Hz, 1H), 6.75 (s, 1H), 6.69 (s, 2H), 6.66 (d, *J* = 5.6 Hz, 1H), 6.37 (dd, *J* = 1.2, 5.6 Hz, 1H), 6.33 (d, *J* = 1.2 Hz, 1H), 6.29 (s, 1H), 5.84 (s, 1H), 5.03 (d, *J* = 8.8 Hz, 1H), 4.83 (d, *J* = 8.8 Hz, 1H), 4.74 (s, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 3.75 (s, 3H), 3.74 (s, 3H), 3.50 (s, 3H), 2.38 (s, 3H), 2.22 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 175.6, 172.7, 166.8, 161.9, 161.6, 149.2, 148.9, 148.5, 137.7, 132.9, 129.5, 128.9, 128.6, 126.9, 125.9, 125.6, 125.2, 121.0, 119.3, 119.0, 118.6, 111.5, 111.2, 109.8, 67.7, 66.1, 56.0, 55.7, 55.4, 55.1, 52.2, 50.8, 46.2, 16.1, 14.1, 13.7. HRMS (ESI, m/z): calcd for $C_{43}H_{42}N_4O_8Na^+$, $[M + H]^+$, 765.2895, found 765.2897.

Methyl 2-((5S,6R,7S,12S,13R)-6,13-bis(3,4-dimethoxyphenyl)-1,11-dimethyl-4,8-dioxo-3,9-diphenyl-2,3,9,10-tetra-azadispiro[4.1.47.25]trideca-1,10-dien-12-yl)acrylate ***(3kb)***. M. p. 184.5–185.5 °C. IR ν_{max} (neat)/cm^{-1}: 2967, 1715, 1706, 1663, 1586, 1507, 1423, 1377, 1265, 1070, 933, 742; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, *J* = 5.2 Hz, 2H), 7.63 (dd, *J* = 0.8, 5.2 Hz, 2H), 7.43 (dt, *J* = 0.8, 5.2 Hz, 2H), 7.35 (t, *J* = 5.2 Hz, 2H), 7.24 (t, *J* = 4.2 Hz, 1H), 7.19 (t, *J* = 5.2 Hz, 1H), 6.78 (d, *J* = 1.2 Hz, 2H), 6.75 (dd, *J* = 1.2, 5.6 Hz, 1H), 6.71 (d, *J* = 5.6 Hz, 1H), 6.65 (d, *J* = 5.6 Hz, 1H), 6.37 (dd, *J* = 0.8, 5.6 Hz, 1H), 6.34 (d, *J* = 1.2 Hz, 1H), 6.31 (s, 1H), 5.76 (s, 1H), 5.53 (d, *J* = 8.8 Hz, 1H), 4.21 (d, *J* = 8.8 Hz, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 3.76 (s, 3H), 3.64 (s, 3H), 3.48 (s, 3H), 2.37 (s, 3H), 2.22 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 175.6, 172.8, 166.6, 163.8, 159.9, 149.2, 149.1, 148.6, 137.8, 137.5, 134.0, 129.6, 128.9, 128.8, 126.7, 125.6, 125.4, 124.8, 121.0, 119.3, 119.2, 118.7, 111.6, 111.3, 110.9, 109.9, 66.9, 66.3, 55.9, 55.8, 55.5, 55.5, 53.6, 51.9, 44.8, 16.5, 13.5. HRMS (ESI, m/z): calcd for $C_{43}H_{42}N_4O_8Na^+$, $[M + H]^+$, 765.2895, found 765.2893.

Methyl 2-((5S,6S,7S,12S,13R)-6,13-bis(4-(dimethylamino)phenyl)-1,11-dimethyl-4,8-dioxo-3,9-diphenyl-2,3,9,10-tetra azadispiro[4.1.47.25]trideca-1,10-dien-12-yl)acrylate ***(3la)***. The reaction was carried out on a 0.2 mmol scale following the **General Procedure**. The annulation product **3la** was purified through column chromatography (hexanes/EtOAc: from 5:1 to 3:1) as white solid (total **3l**: 133 mg, dr = 5:1, 94% yield). M. p. 175.1–176.1 °C. IR ν_{max} (neat)/cm^{-1}: 2947, 2896, 1710, 1622, 1595, 1533, 1489, 1374, 1291, 1228, 947, 850; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, *J* = 0.8 Hz, 2H), 7.49–7.45 (m, 4H), 7.30–7.25 (m, 3H), 7.12 (t, *J* = 4.8 Hz, 1H), 7.03 (d, *J* = 5.2 Hz, 2H), 6.74 (d, *J* = 5.2 Hz, 2H), 6.55 (d, *J* = 6.0 Hz, 2H), 6.51 (d, *J* = 6.0 Hz, 2H), 6.27 (s, 1H), 5.79 (s, 1H), 5.02 (d, *J* = 8.8 Hz, 1H), 4.81 (d, *J* = 8.8 Hz, 1H), 4.72 (s, 1H), 3.73 (s, 3H), 2.87 (s, 6H), 2.81 (s, 6H), 2.37 (s, 3H), 2.25 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 176.0, 172.9, 166.8, 162.2, 161.9, 150.2, 149.7, 137.8, 137.6, 133.1, 129.5, 128.9, 128.8, 128.4, 127.5, 125.5, 125.0, 121.9, 121.0, 119.8, 119.6, 112.6, 112.4, 68.0, 66.4, 54.6, 52.0, 50.7, 46.2, 40.3, 40.2, 16.1, 13.8. HRMS (ESI, m/z): calcd for $C_{43}H_{45}N_6O_4^+$, $[M + H]^+$, 709.3497, found 709.3497.

Methyl 2-((5S,6S,7S,12S,13R)-1,11-dimethyl-6,13-di(naphthalen-1-yl)-4,8-dioxo-3,9-diphenyl-2,3,9,10-tetraazadispiro [4.1.47.25]trideca-1,10-dien-12-yl)acrylate ***(3ma)***. The reaction was carried out on a 0.2 mmol scale following the **General Procedure**. The annulation product **3ma** was purified through column chromatography (hexanes/EtOAc: from 8:1 to 6:1) as white solid (total **3m**: 117 mg, dr = 12:1, 71% yield). M. p. 165.3–166.3 °C. IR ν_{max} (neat)/cm^{-1}: 2978, 2970, 1712, 1701, 1640, 1629, 1501, 1389, 1378, 1256, 1165, 930, 770; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24 (d, *J* =5.6 Hz, 1H), 7.95 (d, *J* = 5.6 Hz, 1H), 7.87 (d, *J* = 5.2 Hz, 2H), 7.82–7.73 (m, 5H), 7.68 (d, *J* = 5.2 Hz, 1H), 7.53–7.28 (m, 10H), 7.15 (t, *J* = 5.2 Hz, 2H), 7.05 (t, *J* = 4.8 Hz, 1H), 6.96 (d, *J* = 5.2 Hz, 1H), 6.41 (d, *J* = 4.8 Hz, 1H), 6.14 (s, 1H), 5.75 (s, 1H), 5.57 (s, 1H), 5.26 (d, *J* =8.8 Hz, 1H), 3.73 (s, 3H), 2.37 (s, 3H), 2.13 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 175.3, 173.6, 166.8, 161.5, 160.4, 137.7, 137.0, 134.2, 133.6, 132.9, 132.8, 131.9, 130.1, 129.4, 129.3, 129.1, 129.0, 129.0, 128.6, 128.3, 127.0, 126.5, 126.1, 126.0, 125.9, 125.7, 125.5, 125.3, 125.1, 124.8, 123.0, 122.2, 120.2, 119.8, 67.2, 66.6, 52.1, 51.5, 47.5, 45.3, 16.5, 14.1. HRMS (ESI, m/z): calcd for $C_{47}H_{39}N_4O_4^+$, $[M + H]^+$, 723.2966, found 723.2961.

Methyl 2-((5S,6S,7S,12S,13R)-1,11-dimethyl-6,13-di(naphthalen-2-yl)-4,8-dioxo-3,9-diphenyl-2,3,9,10-tetraazadispiro [4.1.47.25]trideca-1,10-dien-12-yl)acrylate ***(3na)***. The reaction was carried out on a 0.2 mmol scale following the **General Procedure**. The annulation product **3na** was purified through column chromatography (hexanes/EtOAc: from 8:1 to 6:1) as white solid (total **3n**: 125 mg, dr = 5:1, 87% yield). M. p. 170.8–171.8 °C. IR ν_{max} (neat)/cm^{-1}: 2955, 2870, 1721, 1712, 1658, 1614, 1487, 1363, 1276, 1145, 924, 782; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, *J* =

5.2 Hz, 2H), 7.81 (d, *J* = 5.2 Hz, 1H), 7.77 (d, *J* = 5.2 Hz, 1H), 7.72–7.68 (m, 4H), 7.54–7.53 (m, 3H), 7.45–7.43 (m, 4H), 7.33–7.28 (m, 5H), 7.18–7.16 (m, 2H), 7.05 (d, *J* = 4.4 Hz, 1H), 6.90 (d, *J* = 5.2 Hz, 1H), 6.28 (s, 1H), 5.86 (s, 1H), 5.34 (d, *J* = 8.8 Hz, 1H), 5.10 (d, *J* = 8.8 Hz, 1H), 5.04 (s, 1H), 3.77 (s, 3H), 2.45 (s, 3H), 2.22 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 175.6, 172.7, 166.8, 161.6, 161.5, 137.8, 137.2, 133.2, 133.1, 133.0, 132.9, 132.6, 132.1, 130.8, 129.8, 129.1, 128.5, 128.2, 128.1, 128.0, 127.8, 127.5, 126.6, 126.5, 126.0, 125.9, 125.8, 125.3, 125.1, 124.8, 120.0, 119.5, 67.5, 66.0, 55.4, 52.2, 51.2, 46.3, 16.2, 13.9. HRMS (ESI, m/z): calcd for $C_{47}H_{39}N_4O_4^+$, $[M + H]^+$, 723.2966, found 723.2966.

*Methyl 2-((5S,6S,7S,12S,13S)-6,13-di(furan-2-yl)-1,11-dimethyl-4,8-dioxo-3,9-diphenyl-2,3, 9,10-tetraazadispiro [4.1.47.25]trideca-1,10-dien-12-yl)acrylate (**3oa**).* The reaction was carried out on a 0.2 mmol scale following the **General Procedure**. The annulation product **3oa** was purified through column chromatography (hexanes/EtOAc: from 8:1 to 6:1) as white solid (total **3o**: 115 mg, dr = 13:1, 92% yield). M. p. 178.2–179.2 °C. IR ν_{max} (neat)/cm^{-1}: 2945, 1714, 1595, 1494, 1352, 1315, 1286, 1247, 1011, 795; ^1H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, *J* = 5.2 Hz, 2H), 7.72 (d, *J* = 5.2 Hz, 2H), 7.44–7.40 (m, 4H), 7.24–7.22 (m, 4H), 6.36 (s, 1H), 6.20–6.18 (m, 3H), 5.92 (t, *J* = 1.2 Hz, 1H), 5.79 (s, 1H), 5.36 (d, *J* = 8.4 Hz, 1H), 4.53 (s, 1H), 4.40 (d, *J* = 8.8 Hz, 1H), 3.67 (s, 3H), 2.39 (s, 3H), 2.18 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 174.6, 171.5, 166.3, 162.5, 159.0, 148.1, 147.3, 142.6, 142.4, 137.7, 137.5, 129.0, 128.9, 128.8, 125.5, 125.3, 119.6, 119.2, 110.6, 110.4, 108.2, 107.2, 66.4, 64.3, 51.9, 49.3, 46.9, 45.1, 15.6, 12.9. HRMS (ESI, m/z): calcd for $C_{35}H_{30}N_4O_6Na^+$, $[M + H]^+$, 625.2058, found 625.2060.

*Methyl 2-((5S,6S,7S,12S,13S)-1,11-dimethyl-4,8-dioxo-3,9-diphenyl-6,13-di(thiophen-2-yl)-2,3,9,10-tetraazadispiro[4.1. 47.25]trideca-1,10-dien-12-yl)acrylate (**3pa**).* The reaction was carried out on a 0.2 mmol scale following the **General Procedure**. The annulation product **3pa** was purified through column chromatography (hexanes/EtOAc: from 8:1 to 6:1) as foam solid (125 mg, dr = 11.4:1, 95% yield). IR ν_{max} (neat)/cm^{-1}: 2963, 2891, 1714, 1598, 1510, 1377, 1294, 1261, 1155, 921, 767, 694; ^1H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, *J* = 5.2 Hz, 2H), 7.57 (d, *J* = 5.6 Hz, 2H), 7.46 (t, *J* = 5.2 Hz, 2H), 7.33 (t, *J* = 4.8 Hz, 2H), 7.26 (d, *J* = 5.2 Hz, 1H), 7.17 (t, *J* = 4.8 Hz, 1H), 7.13 (d, *J* = 0.4 Hz, 1H), 7.08 (dd, *J* = 0.8, 3.6 Hz, 1H), 6.93 (d, *J* = 2.4 Hz, 1H), 6.87–6.83 (m, 2H), 6.72 (d, *J* = 2.4 Hz, 1H), 6.35 (s, 1H), 5.91 (s, 1H), 5.35 (d, *J* = 8.8 Hz, 1H), 4.90 (s, 1H), 4.76 (d, *J* = 8.8 Hz, 1H), 3.75 (s, 3H), 2.39 (s, 3H), 2.32 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 174.8, 171.9, 166.5, 160.8, 160.7, 137.6, 137.4, 136.1, 136.0, 132.9, 129.5, 128.9, 128.7, 127.3, 127.0, 126.2, 125.8, 125.7, 125.4, 125.2, 125.0, 119.7, 119.5, 67.5, 67.2, 52.2, 51.1, 47.5, 46.9, 16.0, 13.7. HRMS (ESI, m/z): calcd for $C_{35}H_{30}N_4O_4S_2Na^+$, $[M + H]^+$, 657.1601, found 657.1600.

*Methyl 2-((5S,6R,7R,12S,13S)-1,11-dimethyl-4,8-dioxo-3,9-diphenyl-6,13-di((E)-styryl)-2,3, 9,10-tetraazadispiro[4.1. 47.25]trideca-1,10-dien-12-yl)acrylate (**3qa**).* The reaction was carried out on a 0.2 mmol scale following the **General Procedure**. The annulation product **3qa** and **3qb** were purified through column chromatography (hexanes/EtOAc: from 8:1 to 6:1) as white solid (total **3q**: 113 mg, dr = 1:3.4, 84% yield). M. p. 181.6–182.6 °C. IR ν_{max} (neat)/cm^{-1}: 2970, 2887, 1705, 1660, 1633, 1512, 1388, 1374, 1271, 1149, 946; ^1H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, *J* = 5.2 Hz, 2H), 7.76 (d, *J* = 5.2 Hz, 2H), 7.41 (t, *J* = 5.2 Hz, 2H), 7.36 (d, *J* = 5.2 Hz, 2H), 7.23–7.21 (m, 10H), 6.46 (d, *J* = 11.4 Hz, 2H), 6.40 (d, *J* = 11.4 Hz, 1H), 6.23–6.20 (m, 1H), 6.00 (s, 1H), 5.89 (dt, *J* = 3.2, 11.4 Hz, 1H), 4.48 (d, *J* = 3.2 Hz, 2H), 3.99 (d, *J* = 6.4 Hz, 1H), 3.71 (s, 3H), 2.56 (s, 3H), 2.43 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 175.7, 172.3, 167.7, 166.6, 160.8, 160.3, 137.6, 137.5, 136.1, 135.8, 133.6, 129.5, 128.8, 128.8, 128.6, 128.5, 128.3, 127.9, 126.7, 126.6, 125.6, 125.3, 123.4, 121.8, 119.7, 119.3, 68.4, 66.9, 54.7, 52.1, 51.3, 47.1, 16.5, 13.7. HRMS (ESI, m/z): calcd for $C_{43}H_{39}N_4O_4^+$, $[M + H]^+$, 675.2966, found 675.2966.

*Methyl 2-((5S,6S,7R,12S,13S)-1,11-dimethyl-4,8-dioxo-3,9-diphenyl-6,13-di((E)-styryl)-2,3,9,10-tetraazadispiro[4.1.47. 25]trideca-1,10-dien-12-yl)acrylate (**3qb**).* M. p. 177.4–178.4 °C. IR ν_{max} (neat)/cm^{-1}: 2957, 2862, 1710, 1647, 1612, 1538, 1345, 1353, 1255, 1130, 922; ^1H NMR (400 MHz, $CDCl_3$): δ 7.81 (t, *J* = 4.8 Hz, 4H), 7.42–7.39 (m, 4H), 7.28–7.20 (m, 12H), 6.51 (d, *J* = 11.8 Hz, 1H), 6.47 (s, 1H), 6.39 (d, *J* = 11.4 Hz, 1H), 6.25 (dd, *J* = 6.4, 11.4 Hz, 1H), 5.91 (s, 1H), 5.85 (dd, *J* = 6.0, 11.4 Hz, 1H), 5.04 (d, *J* = 8.4 Hz, 1H), 3.92–3.91 (m, 2H), 3.67 (s, 3H), 2.61 (s, 3H), 2.39 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 175.3, 172.6, 166.6, 161.9, 159.4, 137.5, 136.1, 136.0, 135.7, 135.6, 129.6, 128.9, 128.8, 128.6, 128.5, 128.3, 128.1, 126.7, 126.6, 125.6, 125.3, 122.6, 121.6, 119.8, 119.2, 67.9, 66.9, 54.8, 52.0, 51.8, 46.9, 17.0, 13.2. HRMS (ESI, m/z): calcd for $C_{43}H_{39}N_4O_4^+$, $[M + H]^+$, 675.2966, found 675.2968.

*Methyl 2-((5S,6S,7R,12S,13S)-6,13-dicyclopropyl-1,11-dimethyl-4,8-dioxo-3,9-diphenyl-2,3, 9,10-tetraazadispiro [4.1.47.25]trideca-1,10-dien-12-yl)acrylate (**3rb**).* The reaction was carried out on a 0.2 mmol scale following the **General Procedure**. The annulation product **3rb** was purified through column chromatography (hexanes/EtOAc: from 8:1 to 6:1) as foam solid (105 mg, dr = 1:4.5, 90% yield). IR ν_{max} (neat)/cm^{-1}: 2962, 2876, 1720, 1703, 1618, 1435, 1364, 1287, 1113, 1030, 984, 835, 720; ^1H NMR (400 MHz, $CDCl_3$): δ 7.96 (dd, *J* = 0.8, 5.6 Hz, 2H), 7.77 (dd, *J* = 0.8, 5.6 Hz, 2H), 7.47–7.44 (m, 2H), 7.41–7.38 (m, 2H), 7.25 (t, *J* = 0.8 Hz, 1H), 7.21 (d, *J* = 0.8 Hz, 1H), 6.47 (s, 1H), 5.91 (s, 1H), 4.89 (d, *J* = 8.4 Hz, 1H), 3.73 (s, 3H), 2.60 (s, 3H), 2.40 (dd, *J* = 1.6, 8.4 Hz, 1H), 2.24 (s, 3H), 2.24–2.22 (m, 1H), 1.28–1.27 (m, 1H), 0.73–0.69 (m, 1H), 0.44–0.38 (m, 3H), 0.30–0.26 (m, 1H), 0.06–0.02 (m, 3H), -0.11–(-0.15) (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 176.4, 173.7, 167.0, 162.8, 161.3, 138.0, 137.8, 135.0, 129.4, 128.9, 128.8, 125.3, 125.2, 119.4, 119.2, 67.9, 67.2, 57.7, 52.2, 52.1, 48.0, 16.6, 13.2, 9.4, 9.0, 5.1, 4.4, 2.6, 0.6. HRMS (ESI, m/z): calcd for $C_{33}H_{35}N_4O_4^+$, $[M + H]^+$, 551.2653, found 551.2653.

Gram-scale Synthesis of 3aa and 3ab. To a flame-dried sealable 2-dram vial equipped with a stir bar was added unsaturated pyrazolones **1** (4 mmol, 1 equiv) and MBH ester **1** (1.31 g, 6 mmol, 1.5 equiv) under air. Subsequently untreated $CHCl_3$ (40 mL, *c* = 0.1 M) and triphenylphosphine (105 mg, 0.4 mmol, 10 mol %) were added. The reaction mixture was kept stirring at 22 °C for 2 h until unsaturated pyrazolones **1** was fully consumed (monitored by TLC). Then the organic solvent was removed under reduced pressure and purified through column chromatography (eluent: hexanes: EtOAc = 8: 1 to 5: 1) to afford the desired product **3aa** and **3ab** with total yield of 89%, 2.22 g.

Hydrolysis of Dispiropyrazolone 3aa. To a flame-dried sealable 2-dram vial equipped with a stir bar was added CH_3CN: H_2O (1 mL, 1:1), then NaOH (20 mg, 0.5 mmol, 10 equiv) and dispiropyrazolone **3aa** (31 mg, 0.05 mmol, 1 equiv)

was added in sequence under air. The mixture was warmed up to 60 °C and stirred for 2 h until substrate **3aa** was fully consumed (monitored by TLC). Then the organic solvent was removed under reduced pressure and purified through column chromatography (eluent: hexanes: EtOAc = 5: 1 to 1: 1) to afford the desired product **4** as foam solid (with yield of 87%, 27 mg).

2-((5S, 6S, 7S, 12S, 13R)-1,11-dimethyl-4,8-dioxo-3,6,9,13-tetraphenyl-2,3,9,10-tetraaza dispiro[4.1.47.25]trideca-1,10-dien-12-yl)acrylic acid (4). IR ν_{max} (neat)/cm^{-1}: 3478, 2932, 1735, 1712, 1684, 1576, 1412, 1368, 1163, 873, 728; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, J = 5.2 Hz, 2H), 7.48 (t, J = 5.2 Hz, 2H), 7.42 (d, J = 5.6 Hz, 2H), 7.30–7.27 (m, 3H), 7.25–7.22 (m, 5H), 7.18–7.12 (m, 4H), 6.85 (d, J = 2.4 Hz, 2H), 6.46 (s, 1H), 5.95 (s, 1H), 5.12 (d, J = 8.8 Hz, 1H), 4.88 (d, J = 8.4 Hz, 1H), 4.83 (s, 1H), 2.37 (s, 3H), 2.19 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 175.4, 172.6, 161.5, 137.7, 137.3, 134.7, 133.1, 132.2, 129.2, 129.0, 128.6, 128.5, 128.2, 128.1, 127.8, 126.6, 125.9, 125.3, 119.9, 119.5, 67.7, 66.0, 54.8, 51.0, 45.5, 16.0, 13.9. HRMS (ESI, m/z): calcd for $C_{38}H_{33}N_4O_4^+$, $[M + H]^+$, 609.2496, found 609.2496.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:
NMR spectra (PDF) and X-ray data for **3ja** and **3db**.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENT

This work was supported by the research program from Shanxi Normal University (No. 050502073061 and No. 050502070288) for financial support. The instruments were performed using the Analytical Test Center of Shanxi Normal University, Linfen, China. We also thank Prof. Yun-Long Fu and Dr. Peng-Fei Hao at Shanxi Normal University, for stimulating discussions.

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