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Orthogonal Strapping of *o*-Haloaryl Ynones with Pyrazolones: A One-Pot, Domino Process toward Spiropyrazolones

Mallesh Beesu and Goverdhan Mehta*

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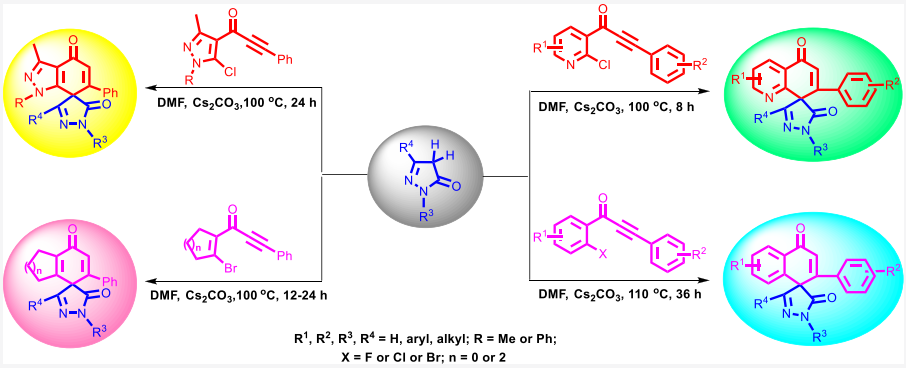

ABSTRACT: A new class of spiroannulated pyrazolone scaffolds have been assembled from diverse *o*-haloaryl ynones and *β*-bromoalkenyl ynones via base mediated, one-pot, metal free, orthogonal strapping (tethering) mediated by the recursive anion(s) derived from pyrazolones. These convenient, preparatively useful transformations proceed through either a tandem Michael addition−intramolecular S_NAr reaction or a tandem Michael addition−intramolecular Ad_NE process to furnish a range of pharmacophoric, diverse, spiroannulated pyrazolones from readily accessible precursors.

Spirocycles embodying different ring sizes and a diverse distribution and combination of heteroatoms are notable for their scaffold diversity, and as a class, they are notable for exhibiting a wide spectrum of biological activities.[1] The distinctive assembly of spirocyclics harboring a unique three dimensionality, build around a quarternary sp^3-carbon center with a sprinkling of rings and heteroatoms, confers on them spatial features amenable for engaging with varied biological targets and receptors.[2] Such spirocyclic constructs, in principle, offer illimitable structural possibilities with significant opportunities for further expanding the chemical space and library creation for mapping their bioactivity potential for pharmaceutical research and drug discovery.[3]

The heteroatom-embellished spirocyclic compounds are also prevalent among many bioactive natural products, and owing to their impressive collective attributes, they have been the targets of both total synthesis and diversity creation compaigns.[4] Among the spirocyclic frameworks, those embodying a pyrazolone segment are of special interest as not only is this compact heterocyclic moiety embedded among natural occurring compounds but also its synthetic variants have applications in pharmaceuticals, agrochemicals, dyes, and as chelating agents of strategic interest.[5] These varied characteristics of pyrazolones render derived spiro-pyrazolones as highly privileged, three-dimensional structural motifs widely encountered among a group of medicinally relevant compounds with various biological activities.[6] In particular, the spiropyrazolones, harboring a spiro-fused six-membered ring and additional appendages, are among well-recognized constructs with a promising bioactivity profile and have drawn considerable traction in recent years from synthetic organic and medicinal chemistry communities.[6,7] Representative examples of biologically active spiropyrazolones with six-membered rings, exhibiting wide ranging biological activities like antimicrobial (**I**),[6a] antitumor (**II**),[6b,d] insecticidal (**III**),[6e] anti-inflammatory (**IV**),[6f] analgesic (**V**),[6g] and phosphodiesterase 4 (PDE4) inhibitor (**VI**)[6h] are displayed in Figure 1.

A confluence of uncommon structural features, possibilities of creative diversification, and expectation of a new or amplified bioactivity spectrum has fueled considerable interest in exploring the chemical space around the six-membered-ring bearing spiropyrazolone scaffold.[5−7] As a result, several synthetic routes, including enantioselective approaches to access these spiropyrazolones motifs have been devised,

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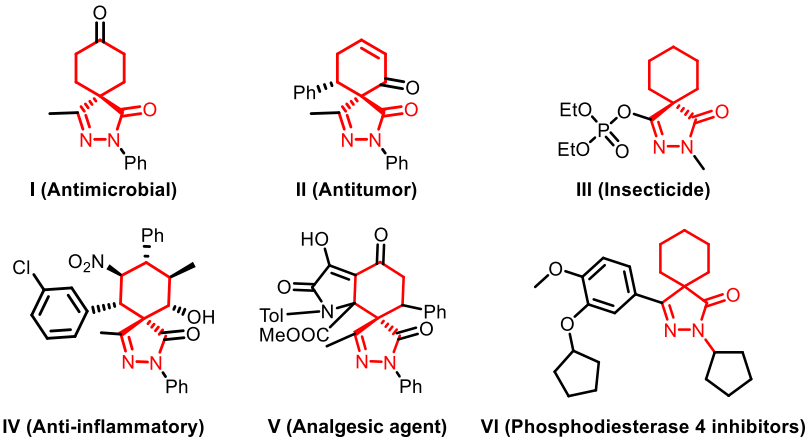
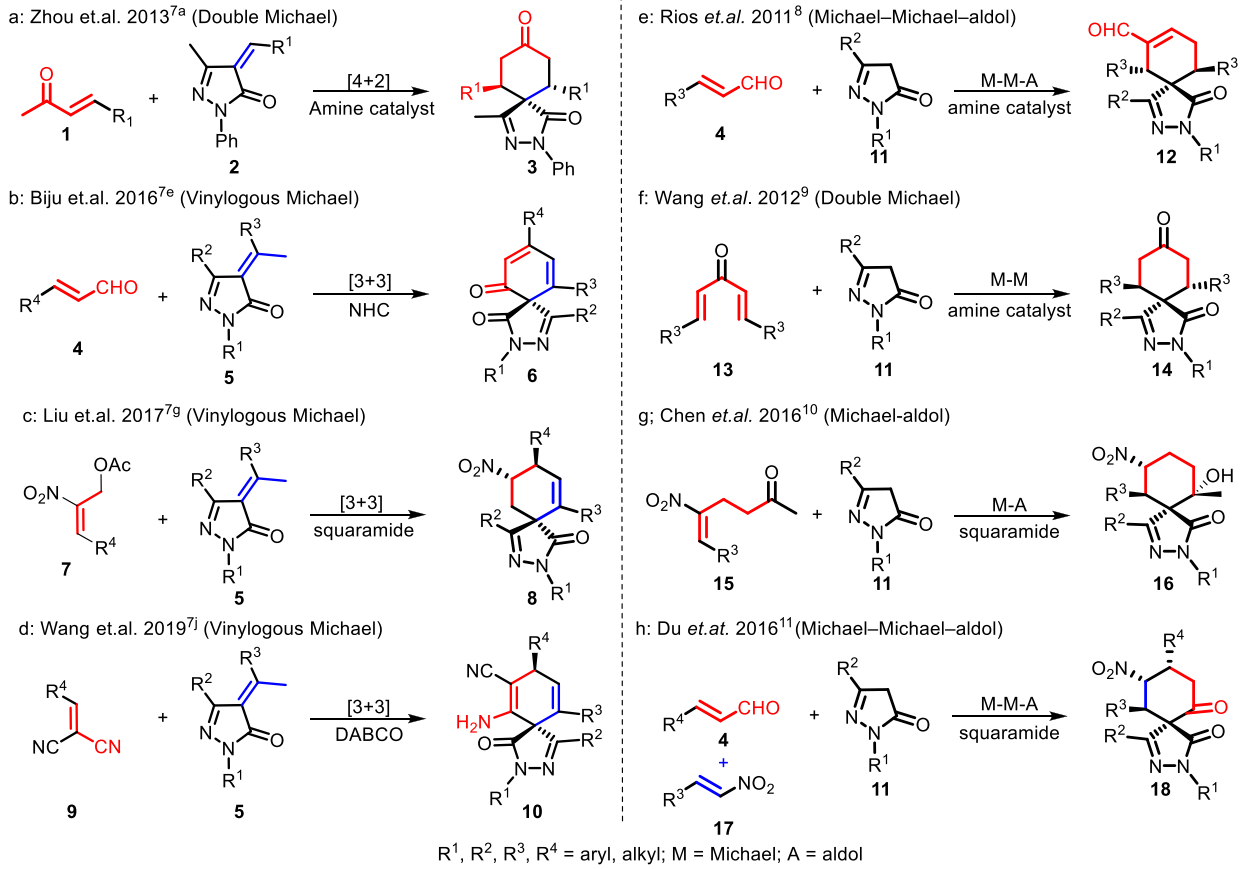


Figure 1. Representative bioactive compounds with a six-membered spiropyrazolone skeleton.

Scheme 1. Selection of Previous Approaches to Six-Membered-Ring Bearing Spiropyrazolones



R^1, R^2, R^3, R^4 = aryl, alkyl; M = Michael; A = aldol

particularly during the past decade.[7−11] At a conceptual level, the commonly pursed approach to spirocyclic pyrazolones has been in the classical mold from readily accessible α-arylidenepyrazolones involving variants of [4+2] cycloaddition and formal [3+3] cycloaddition chemistry via a vinylogous Michael−aldol sequence (Scheme 1a−d).[7] On the other hand, direct approaches toward spirocyclic pyrazolones from easily accessible pyrazolones have received only limited attention, and an assortment of representative efforts in this direction are captured in Scheme 1e−h.[8−11]

While the above-mentioned approaches (Scheme 1) have met with some success, they also necessitate the use of highly reactive partners (double Michael or Michael−aldol acceptors) and fancy bifunctional organocatalysts,[7−11] which in a way, could be self-limiting. Thus, new, practical approaches using readily assembled precursors should be a welcome addition to the repertoire of methods for the synthesis of these valuable scaffolds. Conceptually, recursive anions **B**, sequentially generated from pyrazolones, can be deployed to orthogonally strap *o*-haloaryl ynones **A** through tandem Michael addition−S_NAr reactions, as indicated in Scheme 2, to install a spirocarbon center and generate functionally embellished spirocyclic pyrazolones **C**. An encouraging parallel to this thought process can be found in our recent approach to

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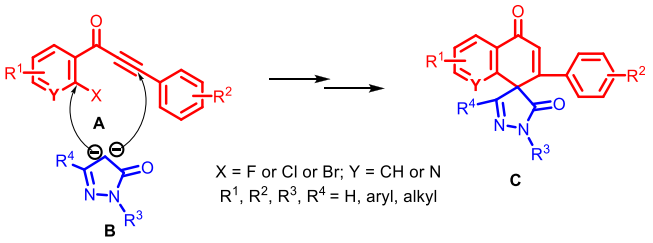
Scheme 2. Conceptualization of a New Strategy toward Spiroannulated Pyrazolones through Aryl Ynone Strapping by Pyrazolone Derived Recursive Anion(s)



spirooxindoles through insertion of oxindoles into *o*-haloaryl ynones.[12a]

An efficient and successful realization of this objective (Scheme 2), leading to an efficient and general method for the spiroannulation of pyrazolones with *o*-haloaryl ynones, through "one-pot" orthogonal strapping via a tandem Michael–S_NAr[12,13] process to deliver a new class of quinolinone- and naphthalenone-annulated spiropyrazolone scaffolds is described here.

For an initial validation of the theme projected in Scheme 2, reaction between *N*-phenyl pyrazolone **11a** and *o*-haloaryl ynone [1-(2-chloropyridin-3-yl)-3-phenylprop-2-yn-1-one] **19a** was probed. The *o*-chloropyridyl ynone **19a** was selected in view of the known propensity of *o*-halopyridyl systems toward facile S_NAr reaction.[12e,13a] Several bases like NaOMe, K_2CO_3, Cs_2CO_3, and DBU were explored for this purpose (see Table S1), but under optimized reaction conditions [Cs_2CO_3 (2.0 equiv), DMF, sealed tube, 100 °C, 8 h], the reaction afforded the expected pyrazolone strapped 3-methyl-1,7′-diphenyl-5′*H*-spiro[pyrazole-4,8′-quinoline]-5,5′(1*H*)-dione (**20a**) in 85% yield (Scheme 3). The structure of quinolone spiropyrazolone **20a** was confirmed unambiguously through a single-crystal X-ray structure determination (Scheme 3).

With this pleasing outcome, we proceeded to demonstrate the generality and scope of this tandem Michael–S_NAr reaction employing various pyrazolones (**11a–f**, see Figure S1) and 2-chloropyridyl ynones (**19a–j**, see Figure S2) under the optimized conditions (16 examples). Reaction between pyrazolones **11a** and various 2-chloropyridyl ynones with donating and withdrawing group appendages (**19b–e**) led to the formation of spiropyrazolones **20b–e**, respectively, in good yields (Scheme 4). Fine tuning of the steric environment, or electronic modulation of the substituent on the ynone moiety, did not have a major effect on the yields under the optimized reaction protocol (**20f–j**, Scheme 4). Similarly, variation in the substitution pattern on the pyrazolone moiety **11b–f** (Figure S1) had some, but not a profound, effect on the formation of tethered products **20k–p** (Scheme 4). The structural integrity of the new spiroannulated products **20a–p** was established through the internally consistent spectral data and single-crystal X-ray structure determination of prototype **20a**.

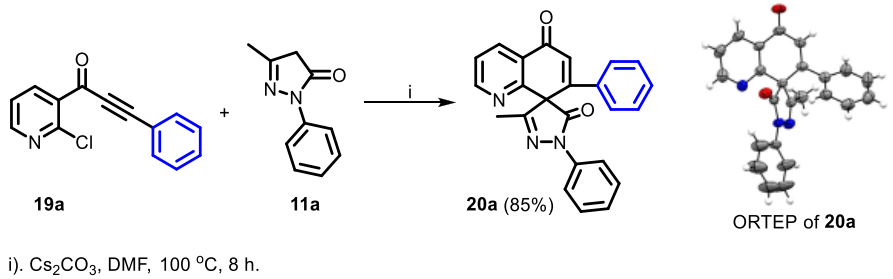
Encouraged by this outcome, it was decided to further explore the generality and scope of this tandem Michael–S_NAr spiroannulation of pyrazolones with *o*-haloaryl ynones. To reinforce confidence in the likely outcome, the first reaction chosen for implementation was the strapping of 2-fluorophenyl ynone **21a** (with 2-fluoro substitution better poised for S_NAr substitution) and pyrazolone **11a**. Indeed, under optimized reaction conditions [Cs_2CO_3 (3.0 equiv), DMF, sealed tube, 110 °C, 36 h; see Table S2], with much longer reaction time, the reaction between 2-fluorophenyl ynones **21a** and pyrazolone **11a** afforded the 3′-methyl-1′,2-diphenyl-4*H*-spiro-[naphthalene-1,4′-pyrazole]-4,5′(1′*H*)-dione **22a** in 75% yield (Scheme 5). It turned out that formation of **22a** proceeded with equal facility when other *o*-halogen-substituted aryl ynones, **21g** (X = Cl) and **21h** (X = Br), were employed. Recourse to bases like K_2CO_3 and solvents like DMF and DMSO also worked, but less efficiently (see Table S2).

The generality of this one-pot spiroannulation of pyrazolones with diverse *o*-haloaryl ynones, **21b–f** (Figure S2), and diverse pyrazolones **11c**, **11d**, and **11f** (Figure S1) could be readily demonstrated to furnish strapped products **22b–j** in moderate to good yields (Scheme 5, 10 examples). The structure of one of them, **22g**, was secured by a single-crystal X-ray structure determination, and its diagnostic spectral signature served as a benchmark for securing other formulations in the series (Scheme 5).

A plausible reaction mechanism for the domino strapping processes through a tandem Michael addition and nucleophilic aromatic substitution (S_NAr) reactions is shown in Scheme 6.[12a] An initial Michael addition of the pyrazolone derived anion to ynone **19**/**21** affords the intermediate **23a**, which tautomerizes to **23b** and in turn displaces the aromatic halide in an S_NAr fashion to deliver the spiroannulated product **20**/**22** via intermediate **23c** (Scheme 6).

Further scoping and contextual amplification of the results displayed in Schemes 3–5 led us to explore strapping of *o*-halo ynones derived from more dense architecture heterocyclic scaffolds with pyrazolones through this tandem Michael–S_NAr protocol to furnish new functionally enriched entities. As an example of this endeavor, we prepared two pyrazolyl ynones **24a** and **24b** following classical methods (Experimental Section). Spiroannulation of 1-(5-chloro-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)-3-phenyl prop-2-yn-1-one (**24a**), and 1-(5-chloro-1,3-dimethyl-1*H*-pyrazol-4-yl)-3-phenylprop-2-yn-1-one (**24b**) with a model pyrazolone **11a** was unexpectedly smooth, and under the optimized reaction conditions [Cs_2CO_3

Scheme 3. Initial Experiment



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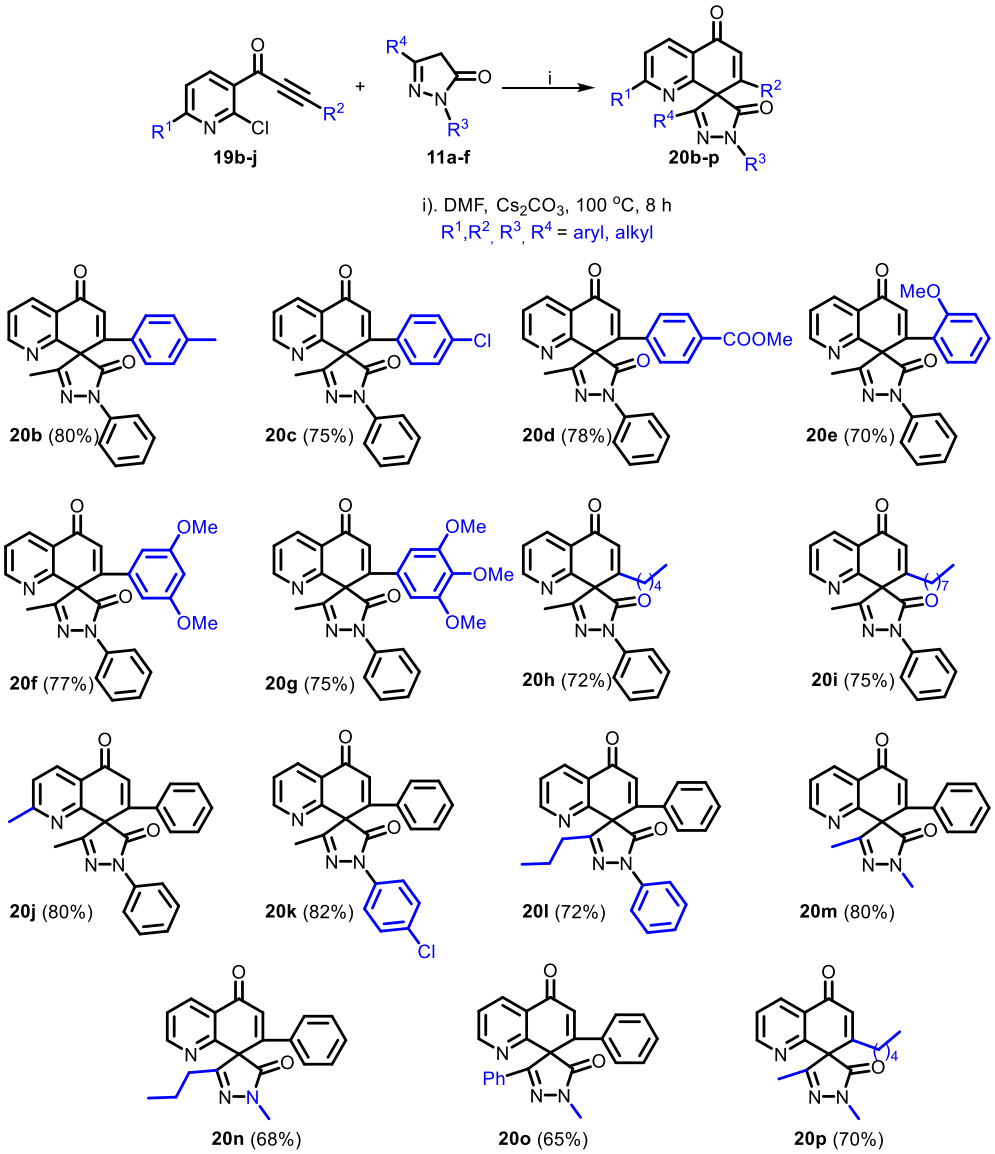
Scheme 4. Reaction of Various Substituted 2-Chloropyridyl Ynones with Pyrazolones



(2.0 equiv), DMF, 100 °C, 24 h] led to functionally embellished spiroannulated pyrazolyl-pyrazolones **25a** and **25b**, respectively, in decent yield (Scheme 7). This brief foray augurs well for further design of more complex and functionally endowed heterocyclic systems based on spiropyrazolones through this "one-pot" Michael–S_NAr protocol for strapping of ynones.

At this stage, a curiosity driven question arose whether our pyrazolone mediated ynone strapping protocol was well suited only for *o*-haloaryl and heteroaryl ynone substrates or can it be extended to nonaromatic *β*-haloalkenyl ynones as well, thereby greatly enhancing the scope of our finding? To answer this question and as a pilot, two carbocyclic *β*-bromoynones **26a** and **26b** were readily assembled.[12a] Exposure of ynones **26a,b** to pyrazolone **11a** under standard reaction conditions led to facile orthogonal strapping to deliver spiroannulated carbocyclic pyrazolones **27a** and **27b** (65% and 75% yields, respectively), embodying a *p*-benzoquinone moiety as well (Scheme 8). The structure of **27a** was established through single-crystal X-ray structure determination, and its spectral signature was used to secure the structure of **27b** (Scheme 8).

A plausible mechanism for the above transformation can be visualized through a tandem Michael addition, followed by addition–elimination (Ad_NE) reactions (**28a** → **28b** → **28c** → **27a**) (Scheme 9).[12a,14] An initial Michael addition of the pyrazolone derived anion to ynone **26a** afforded the intermediate **28a**, which tautomerizes to **28b** and in turn displaces the aromatic halide in an Ad_NE fashion to deliver the spiroannulated product **27a** via intermediate **28c** (Scheme 9).[12a,14]

In conclusion, we have outlined a one-pot, metal-free, orthogonal spiroannulation strategy to conveniently access a new class of quinolinone and naphthalenone annulated spiropyrazolone motifs from readily accessible pyrazolones and *o*-haloaryl ynones. This domino strapping protocol has been further extended to *o*-chloropyrazolyl ynones and *β*-bromocycloalkenyl ynones to deliver some novel heterocyclic and carbocylic spiroannulated scaffolds. We believe that the methodology reported here will enable access to a range of spiroannulated pyrazolone scaffolds for potential biological evaluation and applications.

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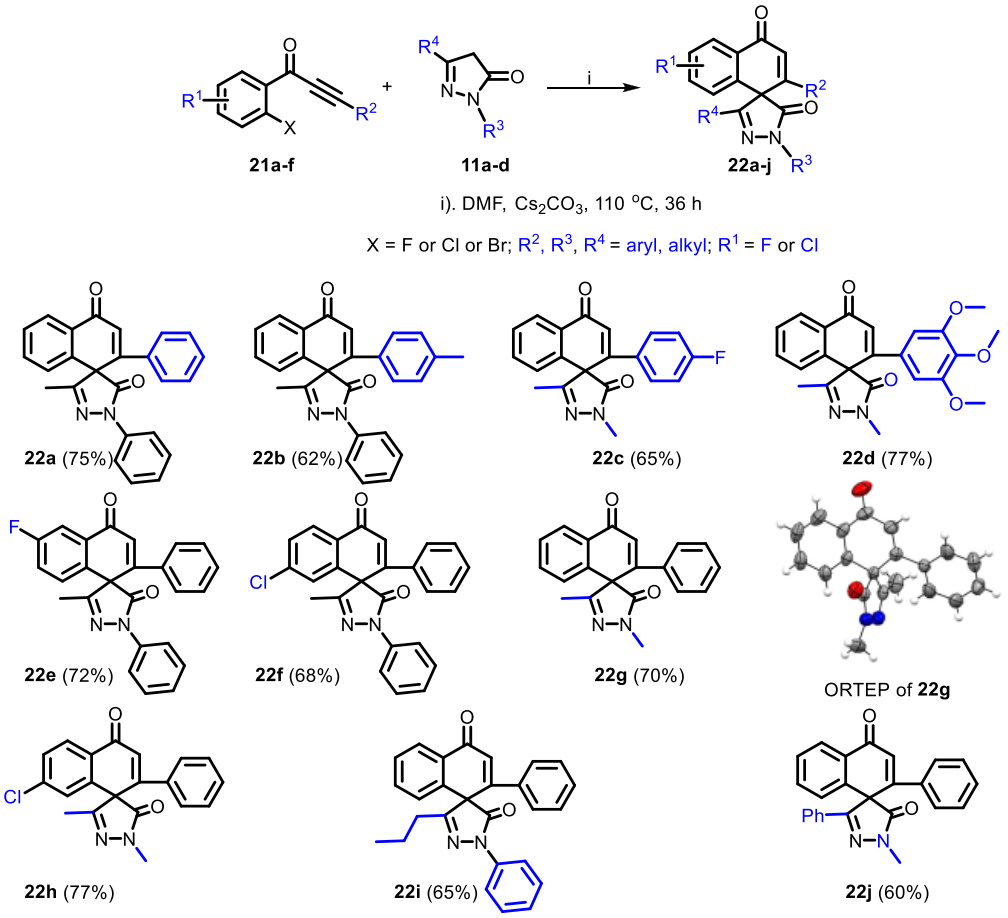
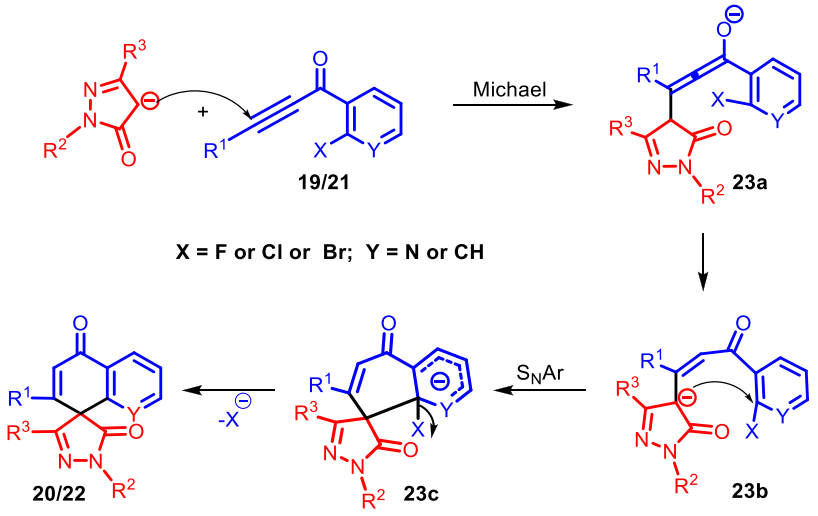
Scheme 5. Reaction of Various Substituted *o*-Haloaryl Ynones with Pyrazolones



Scheme 6. Proposed Reaction Mechanism



EXPERIMENTAL SECTION

General Experimental Details. Unless specified, all reagents were used as obtained from commercial sources. All air and moisture sensitive reactions were performed under N_2 or a blanket in flame- or oven-dried glassware under magnetic stirring. Tetrahydrofuran (THF) was dried over sodium benzophenone ketyl and freshly distilled. Reactions were monitored by TLC (silica gel 60 F254, Merck) with visualization through UV light, iodine, and *p*-anisaldehyde spray. Column chromatographies were on silica gel (60−120 or 100−200 mesh). All solvent extracts were washed with brine and dried over anhydrous Na_2SO_4 prior to concentration under reduced pressure. Melting points were measured on a Buchi B-540 apparatus. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on a 400 or 500 MHz spectrometer at ambient temperature. The coupling constants J are indicated in Hz, and the chemical shifts (δ) are reported in ppm scale downfield from TMS with reference to TMS (δ = 0.0) as internal standard. The signal patterns are indicated as follows: s = singlet, d = doublet, dd = doublet of doublet, t = triplet, q = quartet, m = multiplet. IR spectra were recorded on an FTIR spectrophotometer. High-resolution mass spectra (HRMS) were

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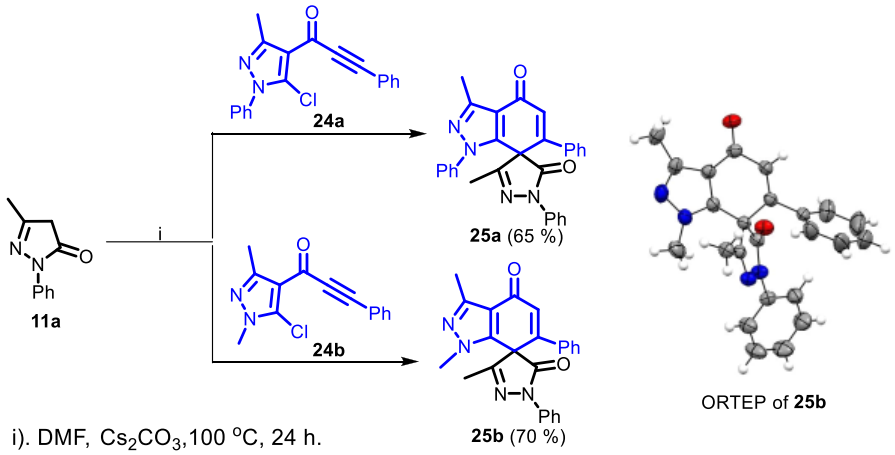
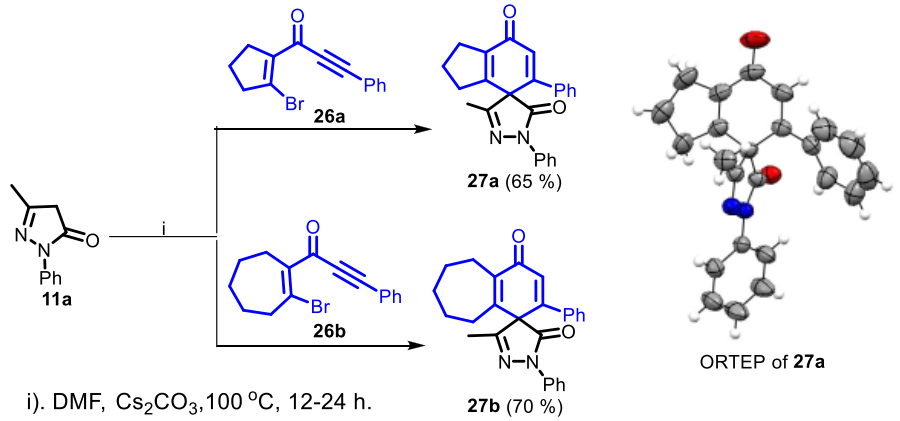
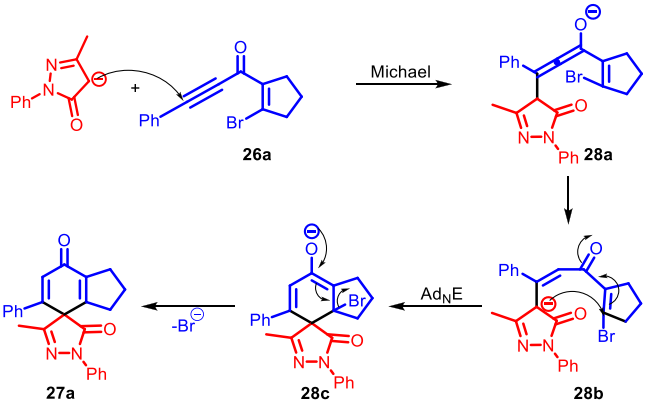
Scheme 7. Spiroannulation of 5-Methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one with *o*-Chloropyrazolyl Ynones



Scheme 8. Spiroannulation of *β*-Bromoalkenyl Ynones with Pyrazolones 11a



Scheme 9. Proposed Reaction Mechanism via Michael–Ad$_N$E Process



recorded using ESI-TOF techniques. Single-crystal X-ray data were collected on a Bruker D8 Quest CCD diffractometer or Oxford XT-Lab Synergy Rigaku diffractometer using Mo Kα radiation at 298 K. Data reduction was carried out with CrysAlispro version 171.33.55 software. Structure solution and refinements were performed with the help of the SHELX2014/7program available in the WinGX package.

Preparation of Pyrazolone and Ynone Precursors. The pyrazolones **11a–f** were known and synthesized by using literature procedures.[15] Among the ynones synthesized by us, **19a–j**, **21a–c**, **21f–h**, and **26a,b** are known, and **21d,e** and **24a,b** are new. Ynones **19a–j**[12e] and **21a–c**,[15d] **21f–h**,[12c] and **26a,b**[12c] were synthesized by following procedures previously reported by us[12c,e] and others,[15d] and the spectral data were matched with the known data. Synthesis and the corresponding spectral data for new compounds (**21d,e** and **24a,b**) are summarized here.

General Procedure for the Preparation of Ynones (21d,e and 24a,b). To a stirred solution of alkyne (2.75 mmol) in anhydrous THF (10 mL) at −78 °C was added *n*-BuLi (2.5 M, 2.75 mmol), and the resulting mixture was stirred at the same temperature for 30 min. Aldehyde (2.5 mmol) in THF (2 mL) was dropwise added, and the reaction temperature was allowed to warm to RT. After completion (TLC), the reaction was quenched with an aq NH_4Cl (10 mL), and H_2O (10 mL) and EtOAc (10 mL) were added. The organic layer was separated and the aqueous layer further extracted with EtOAc (3 × 10 mL). The combined organic phase was washed and concentrated to afford the crude propargyl alcohol, which was used as such for oxidation. To a stirred solution of propargyl alcohol (2.5 mmol) in DMSO (6 mL) at room temperature was added IBX (3 mmol), and the reaction mixture was stirred for 2 h. After completion, the reaction mixture was filtered through a Celite pad, diluted with water (10 mL), and extracted with EtOAc (10 mL × 3). The combined organic layer was washed, dried, and concentrated to furnish a crude product which was purified by column chromatography (eluent, ethyl acetate/hexane, 1:4) to furnish the substituted alkynones (**21d,e** and **24a,b**).

1-(2-Fluorophenyl)-3-(3,4,5-trimethoxyphenyl)prop-2-yn-1-one (21d). Pale yellow solid (629 mg, 80%); mp 166–168 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10–8.07 (m, 1H), 7.60–7.56 (m, 1H), 7.29–7.26 (m, 1H), 7.20–7.16 (m, 1H), 6.89 (s, 2H), 3.89 (s, 3H), 3.88 (s, 6H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 174.2, 162.2 (d, $^1J_{C\text{-}F}$ = 261.4 Hz), 153.4, 141.4, 135.7 (d, $^2J_{C\text{-}F}$ = 9.2 Hz), 131.8, 125.8 (d, $^3J_{C\text{-}F}$ = 7.8 Hz), 124.3 (d, $^4J_{C\text{-}F}$ = 3.8 Hz), 117.2 (d, $^2J_{C\text{-}F}$ = 21.9 Hz), 114.8, 110.7, 93.7 (d, $^4J_{C\text{-}F}$ = 3.3 Hz), 88.2, 61.2, 56.4; IR (neat)

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ν_{max} 2186, 1621, 1500 cm^{-1}; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{18}H_{16}FO_4$315.1027, found 315.1033.

1-(2,5-Difluorophenyl)-3-phenylprop-2-yn-1-one (21e). White solid (454 mg, 75%); mp 75−77 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.77−7.73 (m, 1H), 7.66−7.65 (m, 2H), 7.50−7.47 (m, 1H), 7.42−7.39 (m, 2H), 7.29−7.25 (m, 1H), 7.18−7.13 (m, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 172.9, 158.3 (dd, $^1J_{C\text{-}F}$ = 243.7, $^4J_{C\text{-}F}$ = 0.9 Hz), 158.2 (dd, $^1J_{C\text{-}F}$ = 260.6, $^4J_{C\text{-}F}$ = 5.2 Hz), 133.4, 131.3, 128.8, 126.5 (dd, $^2J_{C\text{-}F}$ = 10.1, $^3J_{C\text{-}F}$ = 6.7 Hz), 122.4 (dd, $^2J_{C\text{-}F}$ = 24.3, $^3J_{C\text{-}F}$ = 9.3 Hz), 119.9, 118.7 (dd, $^2J_{C\text{-}F}$ = 24.9, $^3J_{C\text{-}F}$ = 7.9 Hz), 117.5 (d, $^2J_{C\text{-}F}$ = 25.0 Hz), 94.0 (d, $^4J_{C\text{-}F}$ = 3.5 Hz), 88.33; IR (neat) ν_{max} 2185, 1616, 1484 cm^{-1}; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{15}H_9F_2O$243.0616, found 243.0615.

1-(5-Chloro-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)-3-phenylprop-2-yn-1-one (24a). Yellow solid (624 mg, 78%); mp 77−79 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.64−7.62 (m, 2H), 7.56−7.49 (m, 4H), 7.48−7.44 (m, 2H), 7.40−7.37 (m, 2H), 2.64 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 170.4, 152.5, 137.3, 132.9, 131.7, 130.8, 129.29, 129.27, 128.7, 125.7, 120.3, 118.3, 92.6, 88.4, 15.2; IR (neat) ν_{max} 2198, 1618, 1519, 1489 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{19}H_{13}ClN_2NaO$343.0609, found 343.0628.

1-(5-Chloro-1,3-dimethyl-1*H*-pyrazol-4-yl)-3-phenylprop-2-yn-1-one (24b). Yellow solid (517 mg, 80%); mp 87−89 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, J = 7.7 Hz, 2H), 7.47−7.44 (m, 1H), 7.40−7.37 (m, 2H), 3.82 (s, 3H), 2.54 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 170.1, 151.5, 132.9, 131.9, 130.7, 128.8, 120.4, 117.1, 92.0, 88.2, 36.4, 15.1; IR (neat) ν_{max} 2197, 1606, 1509, 1464 cm^{-1}; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{14}H_{12}ClN_2O$259.0633, found 259.0632.

3-Methyl-1,7′-diphenyl-5′*H*-spiro[pyrazole-4,8′-quinoline]-5,5′(1*H*)-dione (20a). To an oven-dried sealed tube were added ynone **19a** (0.2 mmol, 48.3 mg) and pyrazolone **11a** (0.2 mmol, 35 mg), followed by DMF (2 mL) and Cs_2CO_3 (0.4 mmol, 130 mg). The reaction mixture was placed in a preheated oil bath at 100 °C, and stirred for 8 h. After the consumption of the starting material (TLC), the reaction was quenched with a saturated solution of aq NH_4Cl (10 mL), extracted with EtOAc (3 × 20 mL), worked up, and concentrated. The crude material was purified through silica gel column chromatography (eluent, 60% EtOAC/hexane) to obtain the **20a** as a yellow solid (65 mg, 85%); mp 176−178 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.76 (dd, J = 4.7, 1.9 Hz, 1H), 8.53 (dd, J = 7.9, 1.9 Hz, 1H), 7.84 (dd, J = 8.7, 1.1 Hz, 2H), 7.50 (dd, J = 7.9, 4.7 Hz, 1H), 7.42−7.39 (m, J = 9.1, 5.4, 1.8 Hz, 3H), 7.38−7.33 (m, 4H), 7.24−7.21 (m, 1H), 6.90 (s, 1H), 1.86 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 183.9, 170.0, 159.2, 155.9, 154.1, 152.1, 137.7, 136.4, 135.2, 131.6, 130.4, 129.2, 129.1, 127.3, 126.9, 125.9, 124.5, 119.5, 68.3, 14.9; IR (neat) ν_{max} 1706, 1663, 1578 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{24}H_{17}N_3NaO_2$402.1213, found 402.1210.

Larger-Scale Synthesis of 20a. By following the general procedure, using ynone **19a** (1.5 mmol, 362 mg), pyrazolone **11a** (1.5 mmol, 261 mg), and Cs_2CO_3 (3 mmol, 977 mg), compound **20a** was prepared (470 mg, 83%).

Compounds **20b−p** were synthesized following the procedure for compound **20a**, and their characterization is detailed below.

3-Methyl-1-phenyl-7′-(*p*-tolyl)-5′*H*-spiro[pyrazole-4,8′-quinoline]-5,5′(1*H*)-dione (20b). Yellow solid (63 mg, 80%): mp 174−176 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.76 (dd, J = 4.7, 1.9 Hz, 1H), 8.53 (dd, J = 7.9, 1.9 Hz, 1H), 7.88−7.86 (m, 2H), 7.51−7.48 (m, 1H), 7.44−7.40 (m, 2H), 7.25−7.21 (m, 3H), 7.17−7.15 (m, 2H), 6.90 (s, 1H), 2.34 (s, 3H), 1.84 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 183.9, 170.2, 159.5, 156.1, 154.1, 152.2, 140.8, 137.8, 135.2, 133.6, 131.1, 130.0, 129.1, 127.3, 126.8, 125.8, 124.5, 119.5, 68.3, 21.4, 14.9; IR (neat) ν_{max} 1704, 1660, 1579 cm^{-1}; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{25}H_{20}N_3O_2$394.1550, found 394.1543.

7′-(4-Chlorophenyl)-3-methyl-1-phenyl-5′*H*-spiro[pyrazole-4,8′-quinoline]-5,5′(1*H*)-dione (20c). Yellow solid (62 mg, 75%); mp 180−182 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.77 (dd, J = 4.7, 1.9 Hz, 1H), 8.53 (dd, J = 7.9, 1.9 Hz, 1H), 7.85−7.83 (m, 2H), 7.53−7.50 (m, 1H), 7.44−7.40 (m, 2H), 7.35−7.33 (m, 2H), 7.30−7.27 (m, 2H), 7.26−7.22 (m, 1H), 6.87 (s, 1H), 1.86 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 183.7, 169.9, 159.0, 155.8, 154.3, 150.7, 137.6, 136.7, 135.3, 134.8, 131.9, 129.6, 129.1, 128.3, 127.2, 126.0, 124.6, 119.5, 68.2, 15.0; IR (neat) ν_{max} 1705, 1660, 1579 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{24}H_{16}ClN_3NaO_2$ 436.0823, found 436.0825.

Methyl 4-(3-Methyl-5,5′-dioxo-1-phenyl-1,5-dihydro-5′*H*-spiro[pyrazole-4,8′-quinolin]-7′-yl)benzoate (20d). Yellow solid (68 mg, 78%); mp 185−187 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.77 (dd, J = 4.7, 1.9 Hz, 1H), 8.53 (dd, J = 7.9, 1.9 Hz, 1H), 8.04−8.01 (m, 2H), 7.84−7.81 (m, 2H), 7.53−7.50 (m, 1H), 7.43−7.38 (m, 4H), 7.24−7.20 (m, 1H), 6.90 (s, 1H), 3.90 (s, 3H), 1.86 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 183.6, 169.7, 166.2, 158.7, 155.8, 154.3, 150.9, 140.6, 137.5, 135.2, 132.3, 131.8, 130.4, 129.1, 127.2, 127.1, 126.0, 124.6, 119.5, 68.1, 52.5, 14.9; IR (neat) ν_{max} 1712, 1663, 1579 cm^{-1}; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{26}H_{20}N_3O_4$ 438.1448, found 438.1451.

7′-(2-Methoxyphenyl)-3-methyl-1-phenyl-5′*H*-spiro[pyrazole-4,8′-quinoline]-5,5′(1*H*)-dione (20e). Yellow solid (57 mg, 70%); mp 152−154 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.74 (dd, J = 4.7, 1.9 Hz, 1H), 8.53 (dd, J = 7.9, 1.9 Hz, 1H), 7.81−7.79 (m, 2H), 7.51−7.48 (m, 1H), 7.38−7.31 (m, 3H), 7.21−7.16 (m, 2H), 6.91−6.88 (m, 2H), 6.78 (s, 1H), 3.65 (s, 3H), 1.88 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 184.2, 169.9, 159.5, 156.6, 156.1, 153.7, 149.7, 137.9, 135.2, 133.4, 131.2, 129.7, 129.0, 127.6, 125.5, 125.2, 124.3, 120.8, 119.2, 111.1, 69.1, 55.4, 15.2; IR (neat) ν_{max} 1712, 1655, 1583 cm^{-1}; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{25}H_{20}N_3O_3$410.1499, found 410.1480.

7′-(3,5-Dimethoxyphenyl)-3-methyl-1-phenyl-5′*H*-spiro[pyrazole-4,8′-quinoline]-5,5′(1*H*)-dione (20f). Yellow solid (68 mg, 77%); mp 189−191 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.76 (dd, J = 4.6, 1.8 Hz, 1H), 8.52 (dd, J = 7.9, 1.8 Hz, 1H), 7.92−7.90 (m, 2H), 7.52−7.48 (m, 1H), 7.42−7.38 (m, 2H), 7.23−7.19 (m, 1H), 6.91 (s, 1H), 6.47 (s, 3H), 3.60 (s, 6H), 1.86 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 183.9, 170.1, 161.2, 159.5, 156.0, 154.1, 152.0, 138.3, 137.8, 135.2, 131.4, 129.1, 127.3, 125.8, 124.5, 119.1, 104.7, 102.7, 68.3, 55.4, 15.0; IR (neat) ν_{max} 1700, 1657, 1583 cm^{-1}; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{26}H_{22}N_3O_4$ 440.1605, found 440.1606.

3-Methyl-1-phenyl-7′-(3,4,5-trimethoxyphenyl)-5′*H*-spiro[pyrazole-4,8′-quinoline]-5,5′(1*H*)-dione (20g). Yellow solid (70 mg, 75%); mp 166−168 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.77 (dd, J = 4.7, 1.9 Hz, 1H), 8.53 (dd, J = 7.9, 1.9 Hz, 1H), 7.95−7.92 (m, 2H), 7.53−7.50 (m, 1H), 7.42−7.38 (m, 2H), 7.23−7.20 (m, J = 7.4 Hz, 1H), 6.95 (s, 1H), 6.57 (s, 2H), 3.84 (s, 3H), 3.64 (s, 6H), 1.86 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 183.9, 170.3, 159.9, 156.0, 154.2, 153.6, 151.8, 139.9, 137.9, 135.2, 131.7, 131.0, 129.2, 127.2, 125.8, 124.6, 118.9, 104.0, 68.3, 61.1, 56.2, 15.0; IR (neat) ν_{max} 1701, 1664, 1575 cm^{-1}; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{27}H_{24}N_3O_5$ 470.1710, found 470.1718.

3-Methyl-7′-pentyl-1-phenyl-5′*H*-spiro[pyrazole-4,8′-quinoline]-5,5′(1*H*)-dione (20h). Pale brown liquid (54 mg, 72%); ^1H NMR (500 MHz, $CDCl_3$) δ 8.73 (dd, J = 4.7, 1.9 Hz, 1H), 8.47 (dd, J = 7.9, 1.9 Hz, 1H), 7.98−7.96 (m, 2H), 7.48−7.42 (m, 3H), 7.25−7.22 (m, 1H), 6.72 (s, 1H), 2.29−2.22 (m, 1H), 2.19−2.12 (m, 1H), 1.87 (s, 3H), 1.68−1.62 (m, 2H), 1.34−1.28 (m, 4H), 0.87 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 183.9, 170.4, 159.4, 156.0, 154.3, 154.0, 137.8, 135.0, 129.1, 128.7, 127.5, 125.7, 124.4, 119.2, 68.9, 32.3, 31.3, 26.3, 22.5, 14.6, 14.0; IR (neat) ν_{max} 1715, 1661, 1582 cm^{-1}; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{24}N_3O_2$ 374.1863, found 374.1855.

3-Methyl-7′-octyl-1-phenyl-5′*H*-spiro[pyrazole-4,8′-quinoline]-5,5′(1*H*)-dione (20i). Pale brown liquid (62 mg, 75%); ^1H NMR (500 MHz, $CDCl_3$) δ 8.73 (dd, J = 4.7, 1.9 Hz, 1H), 8.47 (dd, J = 7.9, 1.9 Hz, 1H), 7.98−7.96 (m, 2H), 7.48−7.42 (m, 3H), 7.25−7.22 (m, 1H), 6.71 (s, 1H), 2.29−2.22 (m, 1H), 2.19−2.12 (m, 1H), 1.87 (s, 3H), 1.69−1.58 (m, 2H), 1.33−1.22 (m, 10H), 0.86 (t, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 183.9, 170.4, 159.4, 155.9, 154.3, 153.9, 137.8, 135.0, 129.1, 128.8, 127.5, 125.7, 124.4, 119.2, 68.9, 32.3, 31.8, 29.4, 29.2, 29.1, 26.7, 22.7, 14.6, 14.2;

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IR (neat) ν_{max} 1717, 1664, 1585 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{26}H_{29}N_3NaO_2$ 438.2152, found 438.2152.

2′,3-Dimethyl-1,7′-diphenyl-5′*H*-spiro[pyrazole-4,8′-quinoline]-5,5′(1*H*)-dione (20j). Yellow solid (63 mg, 80%); mp 192−194 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.39 (d, J = 8.1 Hz, 1H), 7.83−7.81 (m, 2H), 7.43−7.38 (m, 3H), 7.35−7.32 (m, 5H), 7.25−7.22 (m, 1H), 6.86 (s, 1H), 2.55 (s, 3H), 1.85 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 184.1, 170.4, 164.4, 159.2, 155.6, 151.7, 137.8, 136.6, 135.0, 131.7, 130.2, 129.2, 129.1, 127.0, 125.9, 124.9, 124.4, 119.8, 68.3, 25.2, 14.9; IR (neat) ν_{max} 1717, 1655, 1590 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{25}H_{19}N_3NaO_2$ 416.1369, found 416.1371.

1-(4-Chlorophenyl)-3-methyl-7′-phenyl-5′*H*-spiro[pyrazole-4,8′-quinoline]-5,5′(1*H*)-dione (20k). Yellow solid (68 mg, 82%); mp 188−190 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.76 (dd, J = 4.7, 1.9 Hz, 1H), 8.53 (dd, J = 7.9, 1.9 Hz, 1H), 7.83−7.80 (m, 2H), 7.53−7.50 (m, 1H), 7.43−7.39 (m, 1H), 7.37−7.34 (m, 4H), 7.32−7.30 (m, 2H), 6.89 (s, 1H), 1.86 (s, 3H); 13C{^1H} NMR (126 MHz, $CDCl_3$) δ 183.8, 170.0, 159.5, 155.8, 154.1, 151.9, 136.3, 136.2, 135.3, 131.7, 130.9, 130.4, 129.3, 129.1, 127.3, 126.9, 124.6, 120.5, 68.3, 15.0; IR (neat) ν_{max} 1710, 1660, 1580 cm^{-1}; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{24}H_{17}ClN_3O_2$ 414.1004, found 414.1043.

1,7′-Diphenyl-3-propyl-5′*H*-spiro[pyrazole-4,8′-quinoline]-5,5′(1*H*)-dione (20l). Yellow solid (59 mg, 72%); mp 134−136 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.76 (dd, J = 4.7, 1.9 Hz, 1H), 8.53 (dd, J = 7.9, 1.9 Hz, 1H), 7.88−7.85 (m, 2H), 7.52−7.48 (m, 1H), 7.43−7.38 (m, 3H), 7.36−7.34 (m, 4H), 7.25−7.21 (m, 1H), 6.91 (s, 1H), 2.15−2.07 (m, 1H), 2.04−1.96 (m, 1H), 1.50−1.37 (m, 2H), 0.76 (t, J = 7.4 Hz, 3H); 13C{^1H} NMR (101 MHz, $CDCl_3$) δ 184.0, 170.2, 162.1, 156.4, 154.0, 152.4, 137.8, 136.5, 135.1, 131.5, 130.4, 129.2, 129.0, 127.2, 127.0, 125.8, 124.5, 119.6, 68.4, 31.3, 18.5, 13.7; IR (neat) ν_{max} 1700, 1657, 1576 cm^{-1}; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{26}H_{22}N_3O_2$408.1707, found 408.1697.

1,3-Dimethyl-7′-phenyl-5′*H*-spiro[pyrazole-4,8′-quinoline]-5,5′(1*H*)-dione (20m). Yellow solid (51 mg, 80%); mp 158−160 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.77 (dd, J = 4.7, 1.9 Hz, 1H), 8.50 (dd, J = 7.9, 1.9 Hz, 1H), 7.50−7.47 (m, 1H), 7.43−7.36 (m, 3H), 7.30−7.27 (m, 2H), 6.82 (s, 1H), 3.36 (s, 3H), 1.76 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 183.9, 171.9, 158.3, 156.0, 154.0, 152.3, 136.5, 135.2, 131.6, 130.2, 129.1, 127.4, 126.9, 124.4, 66.9, 31.9, 14.7; IR (neat) ν_{max} 1700, 1655, 1584 cm^{-1}; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{19}H_{16}N_3O_2$ 318.1237, found 318.1230.

1-Methyl-7′-phenyl-3-propyl-5′*H*-spiro[pyrazole-4,8′-quinoline]-5,5′(1*H*)-dione (20n). Yellow solid (47 mg, 68%); mp 160−162 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.76 (dd, J = 4.7, 1.9 Hz, 1H), 8.49 (dd, J = 7.9, 1.9 Hz, 1H), 7.49−7.46 (m, 1H), 7.42−7.37 (m, 3H), 7.31−7.29 (m, 2H), 6.84 (s, 1H), 3.38 (s, 3H), 2.06−2.00 (m, 1H), 1.93−1.87 (m, 1H), 1.40−1.29 (m, 2H), 0.71 (t, J = 7.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 184.0, 172.0, 161.3, 156.4, 153.9, 152.6, 136.7, 135.1, 131.5, 130.2, 129.0, 127.4, 127.0, 124.3, 67.0, 32.0, 31.1, 18.6, 13.7; IR (neat) ν_{max} 1700, 1664, 1578 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{21}H_{19}N_3NaO_2$ 368.1369, found 368.1332.

1-Methyl-3,7′-diphenyl-5′*H*-spiro[pyrazole-4,8′-quinoline]-5,5′(1*H*)-dione (20o). Pale yellow solid (49 mg, 65%); mp 232−234 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.68−8.66 (m, 1H), 8.57 (dd, J = 7.9, 1.9 Hz, 1H), 7.47−7.43 (m, 1H), 7.40−7.37 (m, 2H), 7.33−7.30 (m, 1H), 7.27−7.18 (m, 5H), 7.12−7.09 (m, 2H), 6.86 (s, 1H), 3.44 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 184.1, 171.2, 157.0, 156.6, 154.3, 154.1, 136.3, 135.5, 131.2, 130.6, 130.4, 129.9, 128.9, 128.7, 127.1, 127.0, 125.8, 124.4, 65.6, 32.4; IR (neat) ν_{max} 1700, 1656, 1582 cm^{-1}; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{24}H_{18}N_3O_2$380.1394, found 380.1392.

1,3-Dimethyl-7′-pentyl-5′*H*-spiro[pyrazole-4,8′-quinoline]-5,5′(1*H*)-dione (20p). Yellow solid (44 mg, 70%); mp 130−132 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.74 (dd, J = 4.7, 1.9 Hz, 1H), 8.45 (dd, J = 7.9, 1.9 Hz, 1H), 7.46 (dd, J = 7.9, 4.7 Hz, 1H), 6.68 (s, 1H), 3.46 (s, 3H), 2.22−2.13 (m, 1H), 2.10−2.01 (m, 1H), 1.76 (s, 3H), 1.64−1.59 (m, 2H), 1.35−1.31 (m, 4H), 0.90 (t, J = 7.0 Hz, 3H); 13C{1H} NMR (126 MHz, $CDCl_3$) δ 184.0, 172.4, 158.8, 156.0, 154.6, 153.9, 135.0, 128.6, 127.7, 124.3, 67.4, 32.1, 32.0, 31.4, 26.3, 22.5, 14.4, 14.0; IR (neat) ν_{max} 1707, 1662, 1580 cm^{-1}; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{18}H_{22}N_3O_2$ 312.1707, found 312.1703.

3′-Methyl-1′,2-diphenyl-4*H*-spiro[naphthalene-1,4′-pyrazole]-4,5′(1′*H*)-dione (22a). To an oven-dried sealed tube were added ynone **21a** (0.2 mmol, 45 mg) and pyrazolone **11a** (0.2 mmol, 35 mg), followed by DMF (2 mL) and Cs_2CO_3 (0.6 mmol, 195 mg). The reaction mixture was placed in a preheated oil bath at 110 °C and stirred for 36 h. After the consumption of the starting material (TLC), the reaction was quenched with a saturated solution of aq NH_4Cl (10 mL), extracted with EtOAc (3 × 20 mL), worked up, and concentrated. The crude material was purified by silica gel column chromatography (eluent, 60% EtOAC/hexane) to obtain **22a** as a pale yellow solid (57 mg, 75%); mp 158−160 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.34−8.32 (m, 1H), 7.84−7.82 (m, 2H), 7.62−7.56 (m, 2H), 7.45−7.41 (m, 2H), 7.40−7.38 (m, 1H), 7.36−7.33 (m, 2H), 7.32−7.29 (m, 2H), 7.27−7.24 (m, 1H), 7.12−7.11 (m, 1H), 6.88 (s, 1H), 1.85 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 184.0, 170.8, 160.9, 150.9, 137.6, 136.7, 135.7, 134.0, 132.2, 131.2, 130.2, 129.6, 129.2, 127.7, 126.9, 126.1, 125.4, 119.5, 65.6, 14.7; IR (neat) ν_{max} 1711, 1656, 1591 cm^{-1}; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{25}H_{19}N_2O_2$ 379.1441, found 379.1438.

Compounds **22b−j** were synthesized following the procedure for compound **22a**, and their characterization is detailed below.

3′-Methyl-1′-phenyl-2-(*p*-tolyl)-4*H*-spiro[naphthalene-1,4′-pyrazole]-4,5′(1′*H*)-dione (22b). Pale yellow solid (49 mg, 62%); mp 172−174 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.33−8.31 (m, 1H), 7.86 (dd, J = 8.7, 1.0 Hz, 2H), 7.61−7.55 (m, 2H), 7.46−7.42 (m, 2H), 7.28−7.24 (m, 1H), 7.21−7.19 (m, 2H), 7.15−7.10 (m, 3H), 6.88 (s, 1H), 2.33 (s, 3H), 1.84 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 183.9, 171.0, 161.2, 150.9, 140.5, 137.7, 135.8, 133.9, 133.8, 131.8, 131.2, 129.9, 129.5, 129.2, 127.7, 126.8, 126.0, 125.3, 119.4, 65.5, 21.4, 14.6; IR (neat) ν_{max} 1713, 1656, 1591 cm^{-1}; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{26}H_{21}N_2O_2$ 393.1598, found 393.1586.

2-(4-Fluorophenyl)-1′,3′-dimethyl-4*H*-spiro[naphthalene-1,4′-pyrazole]-4,5′(1′*H*)-dione (22c). Pale yellow solid (43 mg, 65%); mp 118−120 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.29 (dd, J = 7.7, 1.1 Hz, 1H), 7.62−7.54 (m, 2H), 7.27−7.24 (m, 2H), 7.10−7.07 (m, 2H), 7.00 (d, J = 7.8 Hz, 1H), 6.78 (s, 1H), 3.36 (s, 3H), 1.76 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 183.7, 172.7, 163.8 (d, $^1J_{C-F}$ = 250.9 Hz), 159.8, 149.9, 135.7, 134.0, 132.9 (d, $^4J_{C-F}$ = 3.6 Hz), 132.5, 131.3, 129.5, 129.1 (d, $^3J_{C-F}$ = 8.4 Hz), 127.7, 125.4, 116.2 (d, $^2J_{C-F}$ = 21.7 Hz), 64.4, 31.9, 14.4; IR (neat) ν_{max} 1713, 1659, 1599 cm^{-1}; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{20}H_{16}FN_2O_2$ 335.1190, found 335.1195.

1′,3′-Dimethyl-2-(3,4,5-trimethoxyphenyl)-4*H*-spiro[naphthalene-1,4′-pyrazole]-4,5′(1′*H*)-dione (22d). Pale yellow solid (63 mg, 77%); mp 193−195 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, J = 7.7 Hz, 1H), 7.61−7.53 (m, 2H), 7.01 (d, J = 7.7 Hz, 1H), 6.85 (s, 1H), 6.51 (s, 2H), 3.87 (s, 3H), 3.83 (s, 6H), 3.40 (s, 3H), 1.77 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 184.0, 173.0, 160.6, 153.6, 150.7, 139.7, 135.7, 133.9, 132.2, 131.7, 131.2, 129.4, 127.6, 125.2, 104.3, 64.1, 61.1, 56.3, 32.0, 14.4; IR (neat) ν_{max} 1707, 1658, 1580 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{23}H_{22}N_2NaO_5$429.1421, found 429.1428.

6-Fluoro-3′-methyl-1′,2-diphenyl-4*H*-spiro[naphthalene-1,4′-pyrazole]-4,5′(1′*H*)-dione (22e). Pale yellow solid (57 mg, 72%); mp 125−127 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.98 (dd, J = 8.6, 2.8 Hz, 1H), 7.83−7.81 (m, 2H), 7.45−7.39 (m, 3H), 7.37−7.33 (m, 2H), 7.32−7.24 (m, 4H), 7.12 (dd, J = 8.7, 4.7 Hz, 1H), 6.88 (s, 1H), 1.86 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 182.8, 170.4, 163.1 (d, $^1J_{C-F}$ = 251.5 Hz), 160.5, 151.4, 137.5, 136.4, 133.5 (d, $^3J_{C-F}$ = 7.1 Hz), 131.8, 131.5 (d, $^4J_{C-F}$ = 3.2 Hz), 130.3, 129.3, 129.2, 127.8 (d, $^3J_{C-F}$ = 7.9 Hz), 126.9, 126.2, 121.7 (d, $^2J_{C-F}$ = 23.0 Hz), 119.4, 113.9 (d, $^2J_{C-F}$ = 22.8 Hz), 65.2, 14.6; IR (neat) ν_{max} 1716, 1661, 1593 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{25}H_{17}FN_2NaO_2$419.1166, found 419.1142.

7-Chloro-3′-methyl-1′,2-diphenyl-4*H*-spiro[naphthalene-1,4′-pyrazole]-4,5′(1′*H*)-dione (22f). Pale yellow solid (56 mg, 68%); mp 172−174 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.27 (d, J =

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8.5 Hz, 1H), 7.84−7.82 (m, 2H), 7.55 (dd, J = 8.5, 1.9 Hz, 1H), 7.46−7.38 (m, 3H), 7.36−7.33 (m, 2H), 7.30−7.26 (m, 3H), 7.08 (d, J = 1.9 Hz, 1H), 6.86 (s, 1H), 1.88 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 182.7, 170.2, 160.2, 150.9, 140.6, 137.4, 137.2, 136.4, 132.0, 130.3, 130.2, 129.7, 129.3, 129.2, 126.9, 126.3, 125.4, 119.5, 65.4, 14.7; IR (neat) ν_{max} 1716, 1658, 1590 cm^{-1}; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{25}H_{18}ClN_2O_2$413.1051, found 413.1059.

1′,3′-Dimethyl-2-phenyl-4*H*-spiro[naphthalene-1,4′-pyrazole]-4,5′(1′*H*)-dione (22g). Pale yellow solid (44 mg, 70%); mp 143−145 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.29 (dd, J = 7.8, 1.4 Hz, 1H), 7.62−7.53 (m, 2H), 7.44−7.37 (m, 3H), 7.27−7.25 (m, 2H), 7.01 (dd, J = 7.7, 0.7 Hz, 1H), 6.81 (s, 1H), 3.36 (s, 3H), 1.76 (s, 3H); 13C{1H} NMR (126 MHz, $CDCl_3$) δ 183.9, 172.8, 160.0, 151.1, 136.8, 135.7, 133.9, 132.2, 131.2, 130.0, 129.4, 129.0, 127.6, 126.9, 125.3, 64.2, 31.9, 14.4; IR (neat) ν_{max} 1702, 1656, 1595 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{20}H_{16}N_2NaO_2$339.1104, found 339.1088.

7-Chloro-1′,3′-dimethyl-2-phenyl-4*H*-spiro[naphthalene-1,4′-pyrazole]-4,5′(1′*H*)-dione (22h). Pale yellow solid (54 mg, 77%); mp 179−181 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.23 (d, J = 8.5 Hz, 1H), 7.52 (dd, J = 8.5, 1.9 Hz, 1H), 7.44−7.37 (m, 3H), 7.24−7.22 (m, 2H), 6.97 (d, J = 1.9 Hz, 1H), 6.79 (s, 1H), 3.37 (s, 3H), 1.78 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 182.8, 172.2, 159.4, 151.0, 140.4, 137.2, 136.5, 132.1, 130.2, 130.0, 129.8, 129.2, 129.1, 126.9, 125.4, 64.0, 32.0, 14.5; IR (neat) ν_{max} 1709, 1660, 1588 cm^{-1}; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{20}H_{16}ClN_2O_2$351.0895, found 351.0896.

1′,2-Diphenyl-3′-propyl-4*H*-spiro[naphthalene-1,4′-pyrazole]-4,5′(1′*H*)-dione (22i). Pale yellow solid (53 mg, 65%); mp 148−150 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.33−8.31 (m, 1H), 7.86 (dd, J = 8.7, 1.0 Hz, 2H), 7.61−7.55 (m, 2H), 7.45−7.42 (m, 2H), 7.39−7.37 (m, 1H), 7.36−7.30 (m, 4H), 7.27−7.24 (m, 1H), 7.13−7.12 (m, 1H), 6.89 (s, 1H), 2.14−2.07 (m, 1H), 2.05−1.98 (m, 1H), 1.52−1.45 (m, 2H), 0.78 (t, J = 7.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 183.9, 170.9, 163.9, 151.1, 137.7, 136.8, 136.1, 133.9, 132.1, 131.1, 130.2, 129.5, 129.2, 127.7, 127.0, 126.0, 125.5, 119.5, 65.6, 30.9, 18.5, 13.7; IR (neat) ν_{max} 1714, 1657, 1594 cm^{-1}; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{27}H_{23}N_2O_2$ 407.1754, found 407.1734.

1′-Methyl-2,3′-diphenyl-4*H*-spiro[naphthalene-1,4′-pyrazole]-4,5′(1′*H*)-dione (22j). Pale yellow solid (45 mg, 60%); mp 228−230 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.38−8.36 (m, 1H), 7.55−7.48 (m, 2H), 7.38−7.36 (m, 2H), 7.32−7.27 (m, 2H), 7.24−7.18 (m, 4H), 7.06−7.01 (m, 3H), 6.82 (s, 1H), 3.44 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 184.1, 171.9, 157.6, 153.2, 136.9, 136.6, 133.9, 131.7, 130.8, 130.7, 129.9, 129.6, 129.3, 128.9, 128.6, 127.9, 127.1, 126.1, 125.6, 62.9, 32.4; IR (neat) ν_{max} 1715, 1657, 1596 cm^{-1}; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{25}H_{19}N_2O_2$ 379.1441, found 379.1441.

Compounds **25a**, **25b**, **27a**, and **27b** were synthesized following the procedure for compound **20a**. The reaction time for **27a** was 12 h and **25a**, **25b**, and **27b** was 24 h. Characterization of all compounds is detailed below.

3,3′-Dimethyl-1,1′,6-triphenylspiro[indazole-7,4′-pyrazole]-4,5′(1*H*,1′*H*)-dione (25a). Yellow solid (60 mg, 65%); mp 166−168 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.31−7.23 (m, 10H), 7.21−7.16 (m, 5H), 6.56 (s, 1H), 2.68 (s, 3H), 1.91 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 181.3, 168.1, 155.2, 149.3, 147.3, 142.3, 137.2, 136.7, 135.3, 134.0, 130.4, 129.8, 129.3, 128.8, 128.7, 127.7, 127.2, 126.1, 119.4, 117.4, 62.3, 14.8, 13.4;IR (neat) ν_{max} 1716, 1661, 1493 cm^{-1}; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{29}H_{23}N_4O_2$ 459.1816, found 459.1811.

1,3,3′-Trimethyl-1′,6-diphenylspiro[indazole-7,4′-pyrazole]-4,5′(1*H*,1′*H*)-dione (25b). Yellow solid (55 mg, 70%); mp 185−187 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.66−7.64 (m, 2H), 7.42−7.34 (m, 3H), 7.32−7.29 (m, 2H), 7.27−7.23 (m, 3H), 6.54 (s, 1H), 3.62 (s, 3H), 2.58 (s, 3H), 1.96 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 181.0, 167.5, 155.7, 148.3, 146.5, 140.9, 136.9, 135.4, 134.1, 129.9, 129.3, 128.9, 127.6, 126.6, 119.5, 117.1, 62.1, 36.3, 14.6, 13.3; IR (neat) ν_{max} 1718, 1661, 1498 cm^{-1}; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{24}H_{21}N_4O_2$ 397.1659, found 397.1662.

3′-Methyl-1′,5-diphenyl-2,3-dihydrospiro[indene-4,4′-pyrazole]-5′,7(1*H*,1′*H*)-dione (27a). Brown solid (48 mg, 65%); mp 128−130 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.79−7.77 (m, 2H), 7.44−7.40 (m, 2H), 7.36−7.29 (m, 3H), 7.27−7.25 (m, 3H), 6.71 (s, 1H), 2.83−2.78 (m, 2H), 2.61−2.52 (m, 1H), 2.45−2.35 (m, 1H), 2.13−1.98 (m, 2H), 1.91 (s, 3H); 13C{1H} NMR (101 MHz, $CDCl_3$) δ 184.2, 168.9, 158.1, 152.2, 150.4, 142.5, 137.4, 136.5, 132.8, 130.1, 129.3, 129.2, 126.8, 126.2, 119.5, 66.4, 33.0, 29.6, 21.9, 14.6; IR (neat) ν_{max} 1711, 1653, 1593 cm^{-1}; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{24}H_{21}N_2O_2$ 369.1598, found 369.1557.

3′-Methyl-1′,2-diphenyl-6,7,8,9-tetrahydrospiro[benzo[7]annulene-1,4′-pyrazole]-4,5′(1′*H*,5*H*)-dione (27b). Brown liquid (55 mg, 70%); ^1H NMR (500 MHz, $CDCl_3$) δ 7.71−7.69 (m, 2H), 7.41−7.38 (m, 2H), 7.35−7.31 (m, 1H), 7.29−7.26 (m, 2H), 7.25−7.20 (m, 3H), 6.62 (s, 1H), 2.94−2.89 (m, 1H), 2.69−2.63 (m, 1H), 2.28−2.23 (m, 1H), 2.20−2.15 (m, 1H), 1.95 (s, 3H), 1.89−1.83 (m, 1H), 1.81−1.74 (m, 1H), 1.62−1.53 (m, 4H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 184.8, 169.2, 158.0, 149.6, 149.5, 143.1, 137.3, 136.4, 131.9, 129.8, 129.2, 129.0, 127.1, 126.2, 119.6, 69.1, 32.4, 31.2, 25.5, 25.4, 24.5, 14.9; IR (neat) ν_{max} 1714, 1651, 1595 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{26}H_{24}N_2NaO_2$ 419.1730, found 419.1709.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02087.

Control experiments, and spectra for all new compounds (PDF)

Single-crystal X-ray diffraction data and files for compound **20a** (CCDC 1990420) (CIF)

Single-crystal X-ray diffraction data and files for compound **22g** (CCDC 1990419) (CIF)

Single-crystal X-ray diffraction data and files for compound **25b** (CCDC 1990423) (CIF)

Single-crystal X-ray diffraction data and files for compound **27a** (CCDC 1990425) (CIF)

■ AUTHOR INFORMATION

Corresponding Author

Goverdhan Mehta − *School of Chemistry, University of Hyderabad, Hyderabad 500 046, India;* orcid.org/0000-0001-6841-4267; Email: gmehta43@gmail.com

Author

Mallesh Beesu − *School of Chemistry, University of Hyderabad, Hyderabad 500 046, India*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.joc.0c02087

Notes

The authors declare no competing financial interest.

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