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Gold-Catalyzed Dearomative Spirocyclization of *N*-Aryl Alkynamides for the Synthesis of Spirolactams

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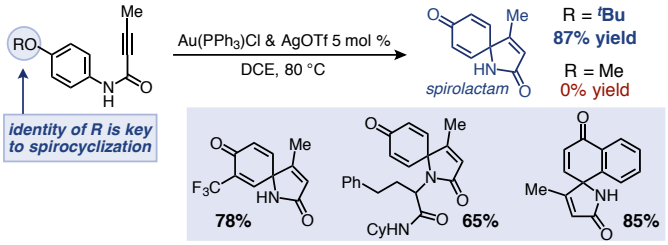


ABSTRACT: A catalytic redox-neutral method for the synthesis of spirolactams proceeding through the dearomative spirocyclization of *N*-aryl alkynamides is reported. As opposed to stoichiometric activating agents employed for related transformation we show that the use of 5 mol % of $Au(PPh_3)Cl$ and AgOTf in dichloroethane at 50-80 °C leads to selective spirocyclization, furnishing the products in yields of 35-87%. The substrate scope of the reaction is good, with both electron-donating and withdrawing groups being tolerated around the arene ring, as well as substitution at the amide nitrogen. The identity of the *para*-alkoxy group on the arene ring is key to achieving selectivity for spirocyclization over alternative mechanistic pathways. While the presence of a *para*-methoxy group leads to trace amounts of the desired spirolactams, the *para*-*tert*-butoxy or *para*-hydroxy substrate analogs furnish the spirolactams in good yield with high selectivity.

Introduction:

The dearomative spirocyclization of substituted phenols and related alkoxyarenes, as a mechanistic paradigm, has inspired the development of a variety of methods for the construction of spirocyclic compounds.[1,2,3,4] Spirocycles have long attracted the attention of organic chemists given the prevalence of spirocyclic scaffolds within natural products. Increasing interest in these compounds can also be seen in the field of medicinal

chemistry given the high degree of three-dimensionality and conformational rigidity spirocyclic motifs impart to compounds.[5]

Of the various classes of compounds capable of undergoing dearomative spirocyclization (**1** → **2**, Figure 1), alkynyl arenes have become popular precursors to an array of functionalized spirocycles.[2] The majority of these methods rely on electrophilic activation of the pendant alkyne by stoichiometric Brønsted acids or halogen electrophiles to induce nucleophilic attack of the arene.[3] In addition, a number of oxidative methods have also been reported.[4] Our group, however, has been interested in the development of redox-neutral catalytic processes (**3** → **6**, Figure 1).[6] The use of mild Lewis acid catalysts for alkyne activation, in place of more traditional alkynophilic reagents, can offer improved atom economy and increased functional group tolerance, thereby granting access to more complex spirocyclic products.

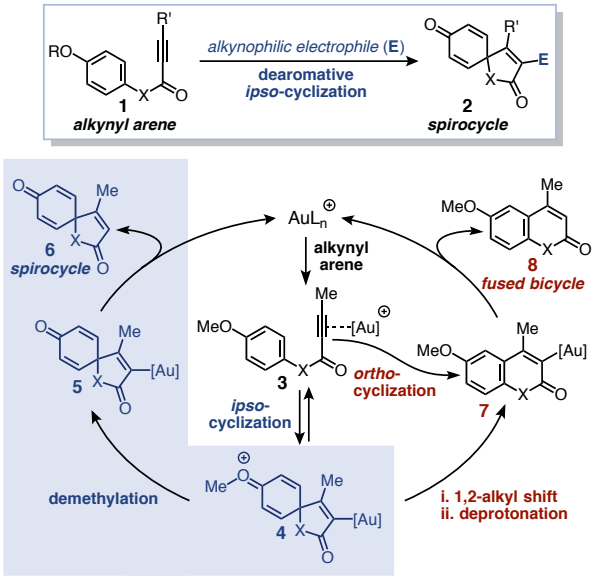


Figure 1. Divergent cyclization pathways of alkynyl arenes

We previously developed an efficient method for the synthesis of spirolactones (**11**, Figure 2) from aryl alkynoate esters (**9**) employing a gold-centered catalyst.[6] Recently, we have begun exploring the reactivity of the analogous *N*-aryl alkynamides (**10**, Figure 2), in an attempt to extend our *ipso*-cyclization method to the synthesis of spirolactams (**6**, X = NH, Figure 1). *Ipso*-cyclization protocols for amide-linked alkynyl arenes

have been developed, including methods proceeding through the action of stoichiometric quantities of acids,[3g] electrophilic halogenating agents,[3c-f] or oxidants for the *in situ* generation of radical activators.[4] However, there have been few reports concerned with redox-neutral catalytic transformation, and those which have been reported include the *ipso*-cyclization event as part of larger cascade processes.[7]

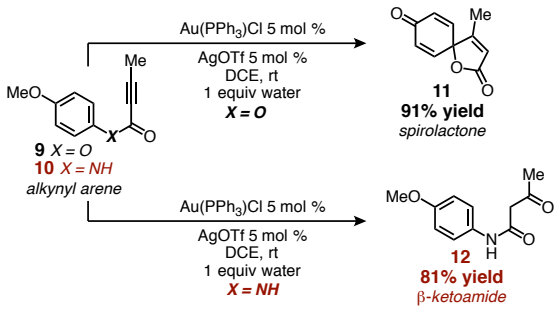


Figure 2. Differing reactivity of alkynyl aryl esters and amides

Here we present our efforts towards the development of a general approach to the synthesis of spirolactams (**6**, X = NH, Figure 1) from readily accessible *N*-aryl alkynamides (**1**, X = NH, Figure 1). While our previously reported ester *ipso*-cyclization conditions failed to deliver the desired spirolactams, even at elevated temperatures, we found that the identity of the arene's *para*-substituent was key to achieving selectivity for the *ipso*-cyclization of these substrates.

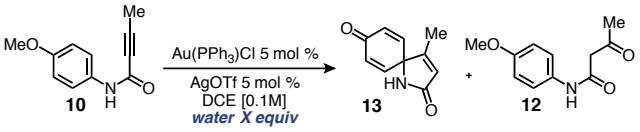
Results and Discussion:

We began our study of *N*-aryl alkynamide *ipso*-cyclization by subjecting amide **10** to our aryl alkynoate ester *ipso*-cyclization conditions: 5 mol % of the catalyst precursor $Au(PPh_3)Cl$ and the silver salt activator AgOTf in dichloroethane (DCE, c = 0.1 M) with one equivalent of water at room temperature (Figure 2). We were surprised to find that the major product of the reaction was the β-ketoamide **12**, which was formed in 81% yield after 24 h, with a trace amount of the target spirolactam **13** observed by crude ^{1}H NMR analysis (entry 1, Table 1). Increasing the reaction temperature to 50 °C failed to yield any improvement (entry 2).

Given the high reaction rate we regularly observed for ester *ipso*-cyclization, with most reactions complete in under an hour, it appeared that the amide substrates were less reactive towards our $Au(PPh_3)Cl$/AgOTf catalyst

system. Similar rate differences for these two substrate classes were also observed in previous studies aimed at *ortho*-cyclization reactions (**3** → **8**, Figure 1).[8] Although the presence of water in the reaction mixture was clearly a problem, the likely outcome of removing water from the reaction mixture was unclear as water proved critical to the selectivity of *ipso*-cyclization over *ortho*-cyclization for the ester substrates. A dramatic decrease in overall percent conversion of amide **10** was observed in the absence of water with β-ketoamide **12** still formed as the major product (entries 3 & 4, Table 1).

Table 1. Attempted *Ipso*-Cyclization With and Without Water[a]



entry	water	T (°C)	% yield:[b] 13	12	(10)
1	1 equivalent	23	4	81	(6)
2	1 equivalent	50	3	78	(5)
3	---	50	>1	35	(58)
4	---	80	>1	28	(60)

[a]All reactions were analyzed after 24 h. [b]^{1}H NMR yields determined using dibenzyl ether as an internal standard.

At this stage, it became clear that that the arene ring was simply not reactive enough to engage the activated alkyne in an *ipso*-cyclization. We revisited our proposed reaction mechanism (Figure 1) and considered ways in which we could modify the reaction to enhance the likelihood of the *ipso*-cyclization event (**3** → **4**) and, furthermore, drive the initial spirocyclic oxocarbenium intermediate to undergo loss of the alkyl group from the *para*-alkoxy substituent (**14** → **15**, Figure 3).

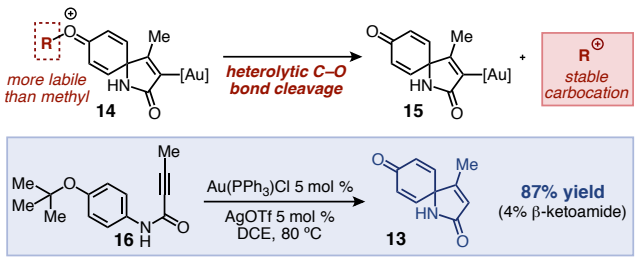
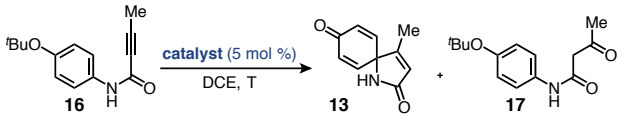


Figure 3. Modifying the *para*-substituent to promote *ipso*-cyclization over alkyne hydration

We speculated that if the substrate was indeed undergoing the necessary *ipso*-cyclization step to reach intermediate **14**, conversion to intermediate **15** might be possible if the methoxy group of the lead substrate **10** was exchanged for a *para*-alkoxy group capable of undergoing heterolytic C–O bond cleavage once in the oxocarbenium state (**14** → **15**). This process would liberate a stable carbocationic species, which could provide a driving force for the overall transformation. The moderate stability of the *tert*-butyl cation led us to synthesize substrate **16**, bearing a *para*-*tert*-butoxy group.

We subjected **16** to 5 mol % of $Au(PPh_3)Cl$ and AgOTf in DCE at 50 °C. Analysis of the reaction mixture by ^{1}H NMR revealed that the spirolactam **13** was formed in 71% yield after 24 h, along with 16% β-ketoamide **17**; 9% of unreacted starting material was also observed. Increasing the reaction temperature to 80 °C further improved the reaction, yielding the spirolactam in 87% yield, with no starting material remaining and only 4% of β-ketoamide observed. Thus, we were able to achieve the selective *ipso*-cyclization of an *N*-aryl alkynamide substrate to the corresponding spirolactam under catalytic conditions in bench-top solvent, by judicious selection of the *para*-alkoxy group.

Table 2. Optimization of *Ipso*-Cyclization Conditions[a]



entry	catalyst	activator	T (°C)	% yield:[b] 13	17	(16)
1	$Au(PPh_3)Cl$	AgOTf	23	16	35	(30)
2	$Au(PPh_3)Cl$	AgOTf	50	71	16	(9)
3[c]	$Au(PPh_3)Cl$	AgOTf	50	54	11	(10)
4	$Au(PPh_3)Cl$	AgOTf	80	**87**	4	(0)
5[c]	$Au(PPh_3)Cl$	AgOTf	80	62	5	(12)
6	$Au(PPh_3)Cl$	$AgSbF_6$	80	45	15	(28)
7	$Au(PPh_3)Cl$	$AgBF_4$	80	35	9	(48)
8	$Au(PPh_3)Cl$	$AgNTf_2$	80	12	15	(56)
9	$Au(XPhos)SbF_6$•MeCN	---	23	10	42	(33)
10	$Au(XPhos)SbF_6$•MeCN	---	50	34	30	(13)
11	$Au(XPhos)SbF_6$•MeCN	---	80	70	9	(0)
12[d]	$Au(PPh_3)Cl$	AgOTf	50	3	82	(0)
13	$Au(PPh_3)Cl$	---	80	0	0	(>99)
14	---	AgOTf	80	0	0	(0)
15	TfOH	---	50	0	0	(12)
16	TfOH	---	80	0	0	(0)

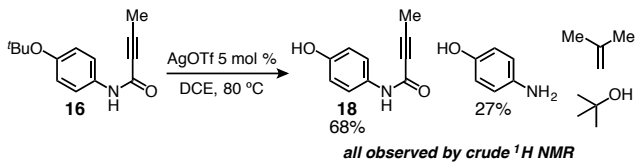
[a]All reactions conducted in DCE (0.1 *M*) and analyzed after 24 h. [b]^{1}H NMR yields determined using dibenzyl ether as an internal standard. [c]DCE (0.2 *M*) [d]1 equiv. of water added.

Having established the identity of the *para*-alkoxy group as a critical structural feature of the substrate with regard to product selectivity, we screened alternative reaction conditions in search of further improvements (Table 2). Changes in the reaction temperature (entry 1), concentration (entries 3 & 5), and the identity of the silver salt activator (entries 6-8) all failed to improve the yield of **13**.

The commercially available cationic gold complex Au(XPhos)SbF_6•MeCN, which we had previously found to be a far superior catalyst to the combination of Au(PPh_3)Cl and AgOTf for the *ortho*-cyclization *N*-aryl alkynamides, gave inferior results for the *ipso*-cyclization reaction (entries 9-11).[8] Interestingly, when we ran the reaction in the presence of water (entry 12), we found a reversal of selectivity back to the β-ketoamide **17**, indicating that the lability of the *tert*-butyl group alone is not enough to achieve *ipso*-cyclization.

In the absence of a silver salt activator, the reaction of **16** with 5 mol % AuPPh_3Cl gave no reaction after 24 h at 80 °C (entry 13). Given that triflic acid can be formed by the reaction of AgOTf with DCE,[9] we ran the reaction in absence of AuPPh_3Cl to test if hidden Brønsted acid catalysis could be responsible for either the *ipso*-cyclization altogether or the cleavage of the *tert*-butyl ether linkage *in situ*, which would generate the *para*-hydroxy substrate analog. Analysis of the crude reaction mixture by ^{1}H NMR showed complete loss of the *tert*-butyl group in 4 h (Scheme 1). While we did not observe any spirolactam or β-ketoamide formation, all of the starting material was consumed. The major product of the reaction was the *para*-hydroxy *N*-aryl alkynamide **18** formed in 68% yield from **16** by cleavage of the *tert*-butyl ether. In addition, 4-hydroxyaniline was formed in 27% yield, presumably by subsequent hydrolysis of **18**. Analysis of the reaction mixture after 24 h showed no further change. The liberation of the *tert*-butyl cation was also supported by the presence of isobutylene and *tert*-butanol in the spectrum.

Scheme 1. *tert*-Butyl ether cleavage by AgOTf in DCE



Finally, we subjected **16** to 5 mol % triflic acid in DCE at both 50 °C and 80 °C (entries 15 & 16). The reaction run at 50 °C contained 12% unreacted starting material, along with a 62% yield of **18**. The reaction run at 80 °C led to a more complex mixture. However, the *para*-hydroxy amide **18** (55%) was clearly detected, along with 5% of 4-hydroxyaniline; no starting material remained. Neither the spirolactam **13**, nor the β-ketoamide **17** were observed.

Collectively, these results suggest that both $AuPPh_3Cl$ and AgOTf are required to form the active catalyst. In addition, while AgOTf is capable of catalyzing the cleavage of the *tert*-butyl ether, either directly or through Brønsted acid catalysis by triflic acid, the resulting *para*-hydroxy substrate **18** is not capable undergoing *ipso*-cyclization in the resulting reaction mixture. Thus, it would appear that the successful catalytic *ipso*-cyclization of *N*-aryl alkynamides requires a highly labile *para*-alkoxy linkage and both $AuPPh_3Cl$ and AgOTf.

With our optimized conditions established, we began to investigate the scope of the *ipso*-cyclization reaction and prepared a series of substrates with varying substituents at the alkynyl position and around the arene ring (**19a-h**, Figure 4). While alkynyl substitution was tolerated, including sterically demanding substituents, phenyl (**19b**) and cyclohexyl (**19d**), the yields of the spirolactams were significantly lower and complex mixtures of byproducts that could not be identified were observed. There was a greater tolerance for substitution around the arene ring. The yields for *ipso*-cyclization of both electron- poor (**19e**, **19f**) and –rich (**19g, 19h**) arenes were moderate to good. Substrate **19h** is particularly noteworthy for the tolerance of an *ortho*-substituent.

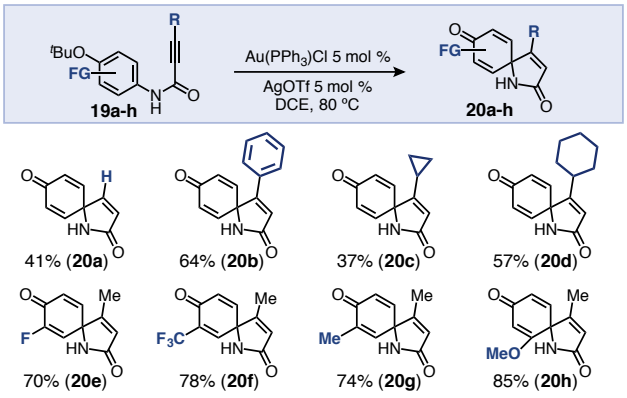


Figure 4. Investigation of *para*-*tert*-butoxy substrates

We next investigated a series of substrates bearing *N*-substitution. Given the general structure of our target substrates we employed an Ugi four-component reaction strategy to synthesize a series of compounds (**21a-c**, Figure 5) that not only exhibited *N*-substitution, but were more complex than those we had previously tested. Related substrates, with a *para*-methoxy group in place of our *tert*-butoxy group, have been shown to under *ipso*-cyclization using stoichiometric activators or strong Brønsted acids.[3f,g] Under our established catalytic conditions, the *para-tert*-butoxy aniline derived Ugi products fared well, giving modest yields of the *N*-substituted spirolactams **22a-c**.

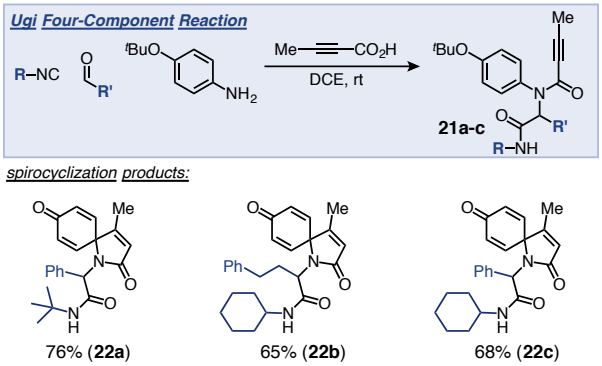


Figure 5. Synthesis and spirocyclization of *N*-substituted *para-tert*-butoxy substrates

Our final investigation of substrate scope was inspired by the *in situ* formation of *para*-hydroxy amide **18** we observed in our control experiments. Since both AgOTf and TfOH were incapable of catalyzing the *ipso*-cyclization of this compound, we were interested to see if our optimized conditions could yield the desired spirolactam product. Given the absence of an alkyl group on the *para*-substituent, we anticipated that this substrate class would be highly reactive. Several *para*-hydroxy substrates (**18**, **23a-f**, Figure 6) were prepared in good yields by selective amine acylation of the *para*-hydroxyaniline precursors.

Overall, these substrates performed very well and delivered the spirolactams (**13**, **24a-f**) in good yields (Figure 6). Given the higher reactivity of this substrate class we were able to decrease the reaction temperature from 80 °C to 50 °C. Experiments run at ambient temperature did provide some product, however, the low solubility of the substrates in DCE led to dramatic decreases in reaction rate, which ultimately culminated in

stalled reactions. Thus, the necessity to heat these reactions is due more so to solvation issues, rather than the inherent reactivity of the substrates themselves. Again, substrates bearing *N*-substitution (**23a**), and both electron-withdrawing (**23b**) and –donating (**23c**) substituents were well tolerated. The selective *ipso*-cyclization of substrate **23c** was somewhat surprising given the increased electron density imparted to the *ortho*-positions of the amide. We suspected that *ortho*-cyclization leading to a 2-quinonlinone product might become a competitive, if not dominant, mode of cyclization for this substrate. However, no 2-quinolinone was detected.

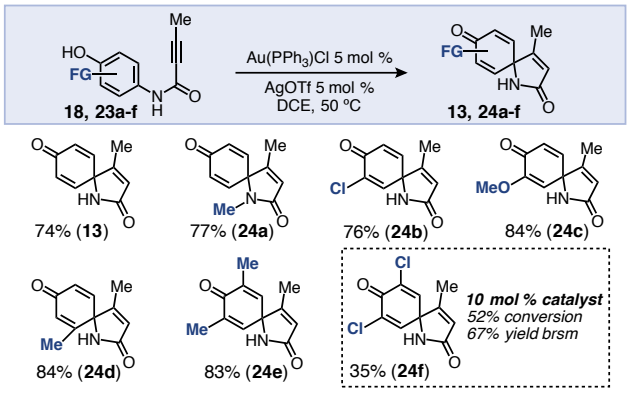
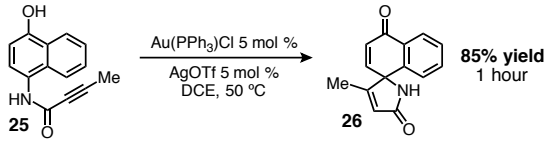


Figure 6. *para*-Hydroxy substrate investigation

The dichloro substrate **23f** was the one outlier in this series. When we analyzed the reaction mixture by GC-MS and ^{1}H NMR after 24 h, only a small amount of spirolactam **24f** was detected. In addition to significant unreacted starting material, we also observed the amide hydrolysis product 3,5-dichloro-4-hydroxyaniline. Increasing the reaction temperature to 80 °C led to complete conversion of the starting material, when analyzed after 24 h, however, the only identifiable product was 3,5-dichloro-4-hydroxyaniline. We re-ran the experiment at 80 °C, this time carefully monitored the progress by GC-MS. We found that after the first 5 h, the product began to decompose at a rate faster than its formation. Increasing the catalyst loading to 10 mol % and stopping the reaction at 5 h allowed us to isolate spirolactam **24f** in 35% yield, along with 48% unreacted starting material.

The final substrate in this series was the aminonaphthol derived *N*-aryl alkynamide **25** (Scheme 2). This substrate proved to be exceptionally reactive, with complete conversion of **25** achieved in 1 h, to give an 85% yield of the benzo-fused spirolactam **26**.

Scheme 2. Naphthyl Derived Substrate Spirocyclization



Conclusion:

In summary, we have developed a catalytic method for the *ipso*-cyclization of *N*-aryl alkynamides, affording spirolactams in moderate to good yields. The successful *ipso*-cyclization of this substrate class is heavily dictated by the identity of the substituent *para* to the alkynamide side-chain. The presence of an alkoxy-group capable of liberating a stable cation is critical to promoting cyclization over hydration of the alkyne. Alternatively, exchanging the *para*-alkoxy group for a hydroxy group yields a class of substrates with increased reactivity, granting access to a wider range of spirolactams from readily accessible starting materials.

Experimental Section:

General Comments

All manipulations of air and/or water sensitive compounds were performed using standard Schlenk techniques. Nitrogen was purified by passage through Drierite. Nuclear Magnetic Resonance spectra were recorded at 300 K on a Bruker 300 MHz Fourier transform spectrometer. ^{1}H NMR spectra recorded in $CDCl_3$ were referenced to TMS (0.00 ppm). Spectra in DMSO-d_6 were referenced to the solvent residual peak (2.50 ppm). 13C{1H} NMR recorded in $CDCl_3$ or DMSO-d_6 were referenced to the residual solvent peak (77.16 ppm and 39.52 ppm respectively). Manual flash column chromatography was conducted on SILICYCLE silica gel (230-400 mesh). Automated flash column chromatography was conducted on a Teledyne ISCO CombiFlash Rf+ system, using RediSep Rf normal-phase silica flash columns. Mass spectra were recorded on a Waters Q-TOF Ultima ESI by the Mass Spectrometry Laboratory of the University of Illinois at Urbana-Champaign. Reactions were monitored by TLC analysis using EtOAc/hexanes mixtures as the eluent and visualized using UV light followed by potassium permanganate stain and/or ceric ammonium molybdate stain.

Part 1. General Procedures for Substrate Synthesis:

Method A - *General procedure for the DIC mediated synthesis of N-aryl alkynamide substrates:* Substrates were prepared by the DIC mediated coupling of the desired aniline derivative with the chosen alkynoic acid catalyzed by DMAP, according to the previously reported conditions.[6,8]

Method B - *General procedure for the isopropyl chloroformate mediated synthesis of N-aryl alkynamides substrates:* Substrates were prepared by reaction of the desired aniline derivative (1.0 equiv) with the mixed carbonic acid anhydride (1.5 equiv) prepared from the chosen alkynoic acid (1.5 equiv) and isopropyl chloroformate (1.5 equiv) with *N*-methyl morpholine (1.5 equiv) in ethyl acetate [0.8 M], according to the previously reported conditions.[6,8]

Method C - *General procedure for the synthesis of N-substituted N-aryl alkynamides substrates via the Ugi four component reaction: para-tert-*Butoxy aniline[10] (1 equiv) was weighed into a round-bottom flask. DCE (0.08 M) was added, followed by the desired aldehyde (1 equiv). The mixture was stirred with a magnetic stir bar at room temperature for 10 minutes, after which 2-butynoic acid (1 equiv) and the desired isocyanide (1 equiv) were added. The mixture was stirred overnight at room temperature. Celite was added to the flask and the solvent was removed by rotary evaporation. The product was then purified by column chromatography to afford the pure amide substrates.

Part 2. Synthesis and Characterization of *N*-Aryl Alkynamide Substrates:

N-(4-Methoxyphenyl)but-2-ynamide **(10). Method B** was followed, using 2-butynoic acid (567.0 mg, 6.7 mmol) and *p*-anisidine (554.2 mg, 4.5 mmol). Extractive work-up followed by automated flash column chromatography on silica gel eluting with a gradient of 0-50% EtOAc/Hex afforded pure amide **10** (544 mg, 64%) as an amorphous white solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.14 (s, 1H), 7.46 (d, J = 8.7 Hz, 2H), 6.83 (d, J = 8.7 Hz, 2H), 3.77 (s, 3H), 1.92 (s, 3H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 156.6, 151.4, 130.8, 121.8, 114.1, 84.3, 75.4, 55.5, 3.7; FT-IR (cm^{-1}) 3270, 3249, 3133, 3073, 3009, 2914, 2240, 1636, 1601, 1548, 1509, 1414, 1241, 1029; HRMS (ES+) *m/z* calcd. for $C_{11}H_{12}NO_2$ $[M+H]^+$ 190.0868, found 190.0871.

N-(4-(tert-Butoxy)phenyl)but-2-ynamide **(16). Method B** was followed, using 2-butynoic acid (1.70 g, 20.25 mmol) and 4-*tert*-butoxyaniline (2.230 g, 13.5 mmol), which was prepared by following known procedure.[11] Following complete consumption of the starting material the solution was washed with 10% HCl (aq), followed by saturated $NaHCO_3$ (aq), and dried over $MgSO_4$. The mixture was filtered, and the volume of the filtrate was reduced by rotary evaporation until precipitation of the product began. The precipitation was further promoted by scratching the walls of the flask with a spatula. The mixture was filtered, and the solid was washed with hexanes and dried under vacuum to afford pure amide **16** (1.62 g, 78%) as a beige amorphous solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.98 (bs, 1H), 7.44 (d, J = 9 Hz, 2H), 6.93 (d, J = 8.7 Hz, 2H), 1.94 (s, 3H), 1.31 (s, 9H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 152.0, 151.2, 133.2, 124.7, 120.8, 84.5, 78.8, 75.4, 28.8, 3.8; FT-IR (cm^{-1}) 3264, 3120, 3053, 2978, 2928, 2236, 1642, 1600, 1535, 1508, 1239, 1161; HRMS (ES+) *m/z* calcd. for $C_{14}H_{18}NO_2$ $[M+H]^+$ 232.1338, found 232.1354.

N-(4-Hydroxyphenyl)but-2-ynamide **(18). Method B** was followed, using 2-butynoic acid (378 mg, 4.5 mmol) and 4-hydroxyaniline (327 mg, 3 mmol). Extractive work-up followed by precipitation and isolation by

filtration afforded pure amide **18** (198 mg, 38%) as an amorphous white solid. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 10.32 (s, 1H), 9.27 (s, 1H), 7.37 (d, J = 9.0 Hz, 2H), 6.69 (d, J = 9.0 Hz, 2H), 2.01 (s, 3H); 13C{1H} NMR (DMSO-d_6, 75 MHz) δ 153.8, 150.1, 130.3, 121.3, 115.1, 83.4, 76.1, 3.2; FT-IR (cm^{-1}) 3358, 2237, 1603, 1515, 1440, 1258; HRMS (ES+) *m/z* calcd. for $C_{10}H_{10}NO_2$ $[M+H]^+$ 176.0712, found 176.0720.

N-(4-(tert-Butoxy)phenyl)propiolamide **(19a). Method A** was followed, using propiolic acid (420.3 mg, 6 mmol) and 4-*tert*-butoxyaniline (661 mg, 4 mmol). Extractive work-up followed by automated flash column chromatography on silica gel eluting with a gradient of EtOAc/Hex 0-40% afforded pure amide **19a** (284 mg, 33%) as an amorphous beige solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.54 (bs, 1H), 7.41 (d, J = 8.7 Hz, 2H), 6.96 (d, J = 8.7 Hz, 2H), 2.92 (s, 1H), 1.33 (s, 9H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 152.5, 149.8, 132.7, 124.8, 121.0, 79.0, 74.2, 28.9; FT-IR (cm^{-1}) 3274, 3119, 3056, 2979, 2111, 1650, 1602, 1535, 1506, 1407, 1366, 1232, 1160; HRMS (ES+) *m/z* calcd. for $C_{13}H_{16}NO_2$ $[M+H]^+$ 218.1181, found 218.1174.

N-(4-(tert-Butoxy)phenyl)-3-phenylpropiolamide **(19b). Method B** was followed, using phenylpropiolic acid (658 mg, 4.5 mmol) and 4-*tert*-butoxyaniline (496 mg, 3 mmol). Extractive work-up followed by automated flash column chromatography on silica gel eluting with a gradient of 0-30% EtOAc/Hex afforded pure amide **19b** (624 mg, 71%) as an amorphous white solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.52 (bs, 1H), 7.53 (d, J = 8.7 Hz, 2H), 7.48 (d, J = 10.2 Hz, 2H), 7.37 (t, J = 7.2 Hz, 1H), 7.27 (t, J = 7.2 Hz, 2H), 6.92 (d, J = 9.0 Hz, 2H), 1.30 (s, 9H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ152.2, 151.3, 133.2, 132.6, 130.2, 128.5, 124.7, 120.9, 120.1, 85.9, 83.6, 78.8, 28.8; FT-IR (cm^{-1}) 3265, 3188, 3166, 3056, 2977, 2122, 1639, 1603, 1540, 1507, 1408, 1368, 1233, 1164; HRMS (ES+) *m/z* calcd. for $C_{19}H_{20}NO_2$ $[M+H]^+$ 294.1494, found 294.1497.

N-(4-(tert-Butoxy)phenyl)-3-cyclopropylpropiolamide **(19c). Method B** was followed, using 3-cyclopropylpropiolic acid (330 mg, 3 mmol) and 4-*tert*-butoxyaniline (330 mg, 2 mmol). Extractive work-up

followed by automated flash column chromatography on silica gel eluting with a gradient of EtOAc/Hex 0-40% afforded pure amide **19c** (314 mg, 61%) as an amorphous beige solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.49 (bs, 1H), 7.39 (d, J = 9 Hz, 2H), 6.94 (d, J = 8.7 Hz, 2H), 1.32 (m, 10H; the 9H of the *tert*-butyl are eclipsing the 1H of the cyclopropyl methine), 0.93-0.88 (m, 4H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 152.0, 151.2, 133.2, 124.8, 120.7, 92.0, 78.8, 71.4, 28.8, 9.07, -0.5; FT-IR (cm^{-1}) 3265, 3193, 3112, 3050, 2977, 2219, 1640, 1603, 1537, 1504, 1402, 1361, 1244, 1164; HRMS (ES+) *m/z* calcd. for $C_{16}H_{20}NO_2$ $[M+H]^+$ 258.1494, found 258.1505.

N-(4-(tert-Butoxy)phenyl)-3-cyclohexylpropiolamide **(19d). Method B** was followed, using 3-cyclohexylpropiolic acid (457 mg, 3 mmol)[11] and 4-*tert*-butoxyaniline (330 mg, 2 mmol). Following complete consumption of the starting material the solution was washed with 10% HCl (aq), followed by saturated $NaHCO_3$ (aq), and dried over $MgSO_4$. The mixture was filtered, and the volume of the filtrate was reduced by rotary evaporation until precipitation of the product began. The precipitation was further promoted by scratching the walls of the flask with a spatula. The mixture was filtered, and the solid was washed with hexanes and dried under vacuum to afford pure amide **19d** (264 mg, 44%) as an amorphous beige solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.63 (bs, 1H), 7.42 (d, J = 8.4 Hz, 2H), 6.94 (d, J = 8.4 Hz, 2H), 2.50 (bm, 1H), 1.82 (bm, 2H), 1.73 (bm, 2H), 1.52 (bm, 3H), 1.32 (s, 12H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 152.1, 133.0, 124.7, 120.7, 92.1, 78.7, 31.7, 28.9, 28.8, 25.6, 24.8; FT-IR (cm^{-1}) 3267, 3115, 3050, 2977, 2931, 2855, 2221, 1640, 1602, 1537, 1506, 1407, 1366, 1320, 1238, 1161; HRMS (ES+) *m/z* calcd. for $C_{19}H_{26}NO_2$ $[M+H]^+$ 300.1964, found 300.1953.

N-(4-(tert-Butoxy)-3-fluorophenyl)but-2-ynamide **(19e). Method B** was followed, using 2-butynoic acid (234 mg, 2.79 mmol) and 3-fluoro-4-*tert*-butoxyaniline (341 mg, 1.86 mmol). Extractive work-up followed by automated flash column chromatography on silica gel eluting with a gradient of EtOAc/Hex 0-40% afforded pure amide **19e** (243 mg, 52%) as an amorphous beige solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.20 (bs, 1H), 7.53

(dd, J = 12 Hz, J = 2.4 Hz, 1H), 7.14 (d, J = 8.7 Hz, 1H), 6.99 (t, J = 8.7 Hz), 1.95 (s, 3H), 1.33 (s, 9H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 158.2, 155.0, 151.3, 139.2, 139.1, 134.1, 134.0, 126.9(2), 126.8(9), 115.1(3), 115.0(9), 109.0, 108.7, 85.1, 80.8, 75.2, 28.4, 3.7; FT-IR (cm^{-1}) 3251, 3117, 3091, 3053, 2977, 2923, 2358, 2339, 2230, 1643, 1596, 1418, 1367, 1116; HRMS (ES+) *m/z* calcd. for $C_{14}H_{17}FNO_2$ $[M+H]^+$ 250.1243, found 250.1249.

N-(4-(tert-Butoxy)-3-(trifluoromethyl)phenyl)but-2-ynamide **(19f). Method B** was followed, using 2-butynoic acid (239 mg, 2.85 mmol) and 3-trifluoromethyl-4-*tert*-butoxyaniline (433 mg, 1.90 mmol). Extractive work-up followed by automated flash column chromatography on silica gel eluting with a gradient of EtOAc/Hex 30-80% afforded pure amide **19f** (243 mg, 43%) as an amorphous white solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.71 (dd, J = 9.0 Hz, J = 2.4 Hz, 1H), 7.56 (d, J = 2.7 Hz, 1H), 7.44 (bs, 1H), 7.16 (d, J = 9.0 Hz, 1H), 2.00 (s, 3H), 1.45 (s, 9H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 151.9, 151.7, 131.4, 125.2, 124.5, 123.5, 123.1, 121.5, 119.2, 119.1, 85.3, 80.9, 75.0, 29.1, 3.6; FT-IR (cm^{-1}) 3434, 2988, 2938, 2240, 2149, 1643, 1544, 1450, 1429, 1324, 1254, 1163, 1133, 1051; HRMS (ES+) *m/z* calcd. for $C_{15}H_{17}F_3NO_2$ $[M+H]^+$ 300.1211, found 300.1209.

N-(4-(tert-Butoxy)-3-methylphenyl)but-2-ynamide **(19g). Method B** was followed, using 2-butynoic acid (295 mg, 3.51 mmol) and 3-methyl-4-*tert*-butoxyaniline (419 mg, 2.34 mmol). Extractive work-up followed by automated flash column chromatography on silica gel eluting with a gradient of EtOAc/Hex 0-40% afforded pure amide **19g** (384 mg, 67%) as a viscous brown oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.29 (d, J = 2.7 Hz, 1H), 7.21 (dd, J = 8.7 Hz, J = 2.7 Hz, 1H), 6.96 (d, J = 8.7 Hz, 1H) 2.22 (s, 3H) 2.00 (s, 3H), 1.36 (s, 9H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 151.3, 151.1, 133.0, 132.2, 122.9, 122.6, 118.1, 84.2, 79.4, 75.6, 29.2, 17.5, 3.9; FT-IR (cm^{-1}) 3267, 3120, 3065, 2981, 2926, 2236, 1639, 1543, 1499, 1415, 1367, 1253, 1173; HRMS (ES+) *m/z* calcd. for $C_{15}H_{20}NO_2$ $[M+H]^+$ 246.1494, found 246.1485.

N-(4-(tert-Butoxy)-3-methoxyphenyl)but-2-ynamide **(19h). Method B** was followed, using 2-butynoic acid (221 mg, 2.63 mmol) and 2-methoxy-4-*tert*-butoxyaniline (1.75 mmol). Extractive work-up followed by automated flash column chromatography on silica gel eluting with a gradient of EtOAc/Hex 0-60% afforded pure amide **19h** (376 mg, 82%) as amorphous white solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.18 (d, J = 9.0 Hz, 1H), 7.84 (bs, 1H), 6.64 (d, J = 2.7 Hz, 1H), 6.59 (dd, J = 9.0 Hz, J = 3.0 Hz, 1H), 3.77 (s, 3H), 2.01 (s, 3H), 1.43 (s, 9H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 156.1, 150.6, 145.5, 125.7, 121.4, 108.8, 107.6, 83.8, 81.3, 75.8, 55.7, 29.2, 4.0; FT-IR (cm^{-1}) 3241, 2916, 2844, 2243, 1636, 1593, 1525, 1307; HRMS (ES+) *m/z* calcd. for $C_{15}H_{20}NO_3$ $[M+H]^+$ 262.1443, found 262.1440.

Amide **21a**. **Method C** was followed, using 4-*tert*-butoxyaniline (100 mg, 0.61 mmol), 2-butynoic acid (54 mg, 0.61 mmol), *tert*-butyl isocyanide (51 mg, 0.61 mmol), and benzaldehyde (65 mg, 0.61 mmol). Extractive work-up followed by automated flash column chromatography on silica gel eluting with a gradient of EtOAc/Hex 0-40% afforded pure amide **21a** (122 mg, 48%) as an amorphous white solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.18-7.14 (m, 5H), 7.02 (bd, J = 6.3 Hz, 2H), 6.77 (d, J = 8.4 Hz, 2H), 5.93 (s, 1H), 5.71 (bs, 1H), 1.66 (s, 3H), 1.34 (s, 9H), 1.27 (s, 9H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 168.3, 155.2, 155.1, 135.1, 134.3, 131.3, 130.5, 128.4, 128.3, 123.9, 91.1, 78.9, 74.2, 65.2, 51.7, 28.8, 28.7, 3.8; FT-IR (cm^{-1}) 3315, 3065, 2971, 2915, 2870, 2249, 1679, 1617, 1504, 1361, 1159; HRMS (ES+) *m/z* calcd. for $C_{26}H_{33}N_2O_3$ $[M+H]^+$ 421.2491, found 421.2472.

Amide **21b. Method C** was followed, using 4-*tert*-butoxyaniline (100 mg, 0.61 mmol), 2-butynoic acid (54 mg, 0.61 mmol), cyclohexyl isocyanide (67 mg, 0.61 mmol), hydrocinnamaldehyde (82 mg, 0.61 mmol). Extractive work-up followed by automated flash column chromatography on silica gel eluting with a gradient of EtOAc/Hex 0-40% afforded pure amide **21b** (107 mg, 37%) as an amorphous beige solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.24-7.13 (m, 5H), 7.07 (d, J = 6.9 Hz, 2H), 6.98 (d, J = 8.7 Hz, 2H), 6.54 (d, J = 8.1 Hz, 1H), 4.94 (t, J = 7.5 Hz, 1H), 3.85-3.75, (m, 1H), 2.68-2.50 (m, 2H), 2.00-1.91 (m, 2H), 1.71-1.57 (m, 9H; the alkynyl methyl

peak is eclipsed by eight of the cyclohexyl protons), 1.36 (s, 9H), 1.28-1.21 (m, 3H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 169.1, 155.9, 155.7, 141.0, 133.5, 130.1, 128.4, 126.1, 124.0, 92.1, 79.1, 73.9, 58.0, 48.2, 32.8, 32.4, 30.2, 28.8, 25.5, 24.7(1), 24.6(5), 3.82; FT-IR (cm^{-1}) 3326, 2973, 2926, 2854, 2249, 1619, 1536, 1504, 1366, 1326, 1160; HRMS (ES+) *m/z* calcd. for $C_{30}H_{39}N_2O_3$ $[M+H]^+$ 475.2961, found 475.2961.

Amide **21c. Method C** was followed, using 4-*tert*-butoxyaniline (100 mg 0.61 mmol), 2-butynoic acid (54 mg, 0.61 mmol), cyclohexyl isocyanide (67 mg, 0.61 mmol), and benzaldehyde (65 mg, 0.61 mmol). Extractive work-up followed by automated flash column chromatography on silica gel eluting with a gradient of EtOAc/Hex 0-40% afforded pure amide **21b** (116 mg, 43%) as an amorphous beige solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.21-7.11 (m, 5H), 7.01 (bd, J = 6.9 Hz, 2H), 6.78 (d, J = 8.1 Hz, 2H), 6.03 (s, 1H), 5.64 (d, J = 7.2 Hz, 1H), 3.88-3.77, (m, 1H), 1.96 (bd, J = 10.5 Hz, 1H), 1.84 (bd, J = 11.7 Hz, 1H), 1.71-1.55 (m, 5H), 1.42-1.31 (m, 3H), 1.28 (s, 9H), 1.19-1.05 (m, 3H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 168.2, 155.3, 155.2, 135.1, 134.3, 131.4, 130.5, 128.6, 128.4, 124.0, 91.2, 79.0, 74.2, 64.7, 48.9, 32.9, 28.9, 25.6, 24.9, 24.8, 3.9; FT-IR (cm^{-1}) 3296, 2974, 2928, 2851, 2254, 1661, 1636, 1505, 1367, 1152; HRMS (ES+) *m/z* calcd. for $C_{28}H_{35}N_2O_3$ $[M+H]^+$ 447.2648, found 447.2639.

N-(4-Hydroxyphenyl)-N-methylbut-2-ynamide **(23a). Method B** was followed, using 2-butynoic acid (378 mg, 4.5 mmol) and (4-methylamino)phenol hemisulfate (517mg, 3 mmol). Extractive work-up followed by precipitation and isolation by filtration afforded pure amide **23a** (261 mg, 46%) as an amorphous white solid. Spectroscopic analysis revealed this product to be a mixture of atropisomers. The data reported here is for the major isomer. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 9.64 (bs, 1H), 7.12 (d, J = 8.1 Hz, 2H), 6.77 (d, J = 8.1 Hz, 2H), 3.12 (s, 3H), 1.74 (s, 3H); 13C{1H} NMR (DMSO, 75 MHz) δ 156.7, 153.3, 134.3, 128.4, 115.5, 89.3, 74.4, 36.2, 3.2; FT-IR (cm^{-1}) 3182, 2917, 2230, 1615, 1514, 1448, 1390, 1266, 1234, 1168, 1099; HRMS (ES+) *m/z* calcd. for $C_{11}H_{12}NO_2$ $[M+H]^+$ 190.0868, found 190.0862.

N-(3-Chloro-4-hydroxyphenyl)but-2-ynamide **(23b). Method B** was followed, using 2-butynoic acid (378 mg, 4.5 mmol) and 3-chloro-4-hydroxyaniline (431 mg, 3 mmol). Extractive work-up followed by precipitation and isolation by filtration afforded pure amide **23b** (448 mg, 71%) as an amorphous white solid. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 10.53 (s, 1H), 10.05 (s, 1H), 7.69 (d, J = 2.4 Hz, 1H), 7.33 (dd, J = 8.7 Hz, J = 2.4 Hz, 1H), 6.93 (d, J = 9.0 Hz, 1H), 2.06 (s, 3H); 13C{1H} NMR (DMSO-d_6, 300 MHz) δ 150.2, 149.4, 131.0, 121.0, 119.6, 119.1, 116.5, 84.1, 75.8, 3.2; FT-IR (cm^{-1}) 3319, 3127, 2234, 1626, 1595, 1549, 1493, 1263; HRMS (ES+) *m/z* calcd. for $C_{10}H_9ClNO_2$ $[M+H]^+$ 210.0322, found 210.0314.

N-(4-Hydroxy-3-methoxyphenyl)but-2-ynamide **(23c). Method B** was followed, using 2-butynoic acid acid (378 mg, 4.5 mmol) and 3-methoxy-4-hydroxyaniline (417 mg, 3 mmol). Extractive work-up followed by precipitation and isolation by filtration afforded pure amide **23c** (418 mg, 68%) as an amorphous white solid. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 10.34 (s, 1H), 8.83 (s, 1H), 7.29 (s, 1H), 6.99 (d, J = 8.1 Hz, 1H), 6.71 (d, J = 8.1 Hz, 1H), 3.75 (s, 3H), 2.05 (s, 3H); 13C{1H} NMR (DMSO-d_6:$CDCl_3$ (3:1), 300 MHz) δ 150.0, 147.2, 143.0, 130.7, 115.1, 112.2, 105.0, 83.2, 76.1, 55.5, 3.2; FT-IR (cm^{-1}) 3295, 2938, 2234, 1621, 1516, 1274; HRMS (ES+) *m/z* calcd. for $C_{11}H_{12}NO_3$ $[M+H]^+$ 206.0817, found 206.0821.

N-(4-Hydroxy-2-methylphenyl)but-2-ynamide **(23d). Method B** was followed, using 2-butynoic acid (252 mg, 3 mmol) and 2-methyl-4-hydroxyaniline (246 mg, 2 mmol). Extractive work-up followed by automated flash column chromatography on silica gel eluting with a gradient of EtOAc/Hex 0-60% afforded pure amide **23d** (185 mg, 49%) as an amorphous tan solid. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 9.72 (s, 1H), 9.29 (s, 1H), 6.96 (d, J = 8.7 Hz, 1H), 6.59 (d, J = 2.7 Hz, 1H), 6.54 (dd, J = 8.4 Hz, J = 2.4 Hz, 1H), 2.06 (s, 3H), 2.01 (s 3H); 13C{1H} NMR (DMSO, 75 MHz) δ 155.5, 151.3, 134.4, 127.3, 126.5, 116.6, 112.7, 83.3, 75.9, 17.9, 3.2; FT-

IR (cm^{-1}) 3203, 2975, 2923, 2239, 1586, 1528, 1503, 1454, 1424, 1300, 1220; HRMS (ES+) *m/z* calcd. for $C_{11}H_{12}NO_2$ $[M+H]^+$ 190.0868, found 190.0877.

N-(4-Hydroxy-3,5-dimethylphenyl)but-2-ynamide **(23e). Method B** was followed, using 2-butynoic acid (378 mg, 4.5 mmol) and 3,5-dimethyl-4-hydroxyaniline (412 mg, 3 mmol). Extractive work-up followed by precipitation and isolation by filtration afforded pure amide **23e** (340 mg, 56%) as an amorphous white solid. ^1H NMR (DMSO-d_6, 300 MHz) δ 10.24 (s, 1H), 8.12 (s, 1H), 7.17 (s, 1H), 2.15 (s, 6H), 2.05 (3H); 13C{1H} NMR (DMSO-d_6, 75 MHz) δ 150.0, 149.6, 130.3, 124.4, 119.9, 83.3, 76.2, 16.8, 3.2; FT-IR (cm^{-1}) 3233, 3034, 2956, 2916, 2852, 2231, 1623, 1538, 1483, 1284, 1200; HRMS (ES+) *m/z* calcd. for $C_{12}H_{14}NO_2$ $[M+H]^+$ 204.1025, found 204.1021.

N-(3,5-Dichloro-4-hydroxyphenyl)but-2-ynamide **(23f). Method B** was followed, using 2-butynoic acid (378 mg, 4.5 mmol) and 3,5-dichloro-4-hydroxyaniline (534 mg, 3 mmol). Extractive work-up followed by precipitation and isolation by filtration afforded pure amide **23f** (322 mg, 44%) as an amorphous white solid. ^1H NMR ($CDCl_3$, 300 MHz) δ 7.49 (s, 2H), 7.31 (bs, 1H), 5.76 (s, 1H), 2.01 (s, 3H); 13C{1H} NMR ($CDCl_3$, 300 MHz) δ 151.0, 145.2, 130.7, 121.3, 120.2, 85.6, 75.0, 4.0; FT-IR (cm^{-1}) 3272, 2238, 1642, 1492, 1271, 1162; HRMS (ES+) *m/z* calcd. for $C_{10}H_8Cl_2NO_2$ $[M+H]^+$ 243.9932, found 243.9940.

N-(4-Hydroxynaphthalen-1-yl)but-2-ynamide **(25). Method B** was followed, using 2-butynoic acid (378 mg, 4.5 mmol) and 4-amino-naphthalen-1-ol (478 mg, 3 mmol). Extractive work-up followed by precipitation and isolation by filtration afforded pure amide **25** (409 mg, 61%) as an amorphous brown solid. ^1H NMR (DMSO-d_6, 300 MHz) δ 10.27 (s, 1H), 10.23 (s, 1H), 8.14 (dd, J = 8.4 Hz, J = 1.2 Hz, 1 H), 7.78 (d, J = 7.8 Hz, 1H), 7.55-7.44 (apparent multiplet, 2H), 7.25 (d, J = 8.1 Hz, 1H), 6.83 (d, J = 8.1 Hz, 1H), 2.06 (s, 3H); 13C{1H}

NMR (DMSO, 75 MHz) δ 157.2, 157.1, 135.0, 131.5, 129.9(3), 129.8(9), 129.5, 128.7, 127.9, 127.5, 112.4, 89.0, 81.1, 8.4; FT-IR (cm^{-1}) 3289, 3149, 2236, 1610, 1577, 1307, 1274; HRMS (ES+) *m/z* calcd. for $C_{14}H_{12}NO_2$ $[M+H]^+$ 226.0868, found 226.0866.

Part 3. General Spirocyclization Procedure for *N*-Aryl Alkynamides:

To a 4 mL vial was added AgOTf (5 mol %), followed by $Au(PPh_3)Cl$ (5 mol %) and a Teflon coated micro stir bar. Bench-top DCE (0.1 M) was then added and the mixture was set to stir at room temperature for 2 minutes. Lastly the *N*-aryl alkynamide substrate was added and the vial was capped with a Teflon lined screw cap and set to stir at room temperature or placed into an aluminum heating block pre-heated to 50 or 80 ºC. Upon complete consumption of the starting material as judged by TLC (developing with mixtures of EtOAc in hexanes) or GC-MS the vial was cooled to room temperature. The reaction mixture was concentrated onto Celite via rotary evaporation and chromatographed by flash column chromatography on silica gel eluting with mixtures of EtOAc and hexanes.

Part 4. Characterization of Products:

N-(4-(methoxy)phenyl)-3-oxobutanamide **(12).** A modification of the **General Spirocyclization Procedure** was followed. Into a 4 mL vial was added AgOTf (2.6 mg, 5 mol %), $Au(PPh_3)Cl$ (4.9 mg, 5 mol %), a Teflon coated micro stir bar, DCE (2 mL, 0.1M), and water (3.6 uL, 0.2 mmol, 1 equiv.). The mixture was stirred vigorously at room temperature for 2 minutes, after which the amide substrate **10** (38 mg, 0.2 mmol) was added. Upon consumption of the starting material the reaction was concentrated onto Celite and purified via automated flash column chromatography on silica gel eluting with a gradient of 0-70% EtOAc/Hex to afford **12** (33.5 mg, 81%) as an amorphous white solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.02 (bs, 1H), 7.43 (d, J = 7.5 Hz, 2H), 6.85 (d, J = 7.5 Hz, 2H), 3.78 (s, 3H), 3.56 (s, 2H), 2.31 (s, 3H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 205.3, 163.7, 156.7, 130.7, 122.1, 114.2, 55.5, 49.9, 31.3; FT-IR (cm^{-1}) 3249, 3135, 3076, 2956, 2922, 1717, 1652, 1607, 1547, 1518, 1410, 1320, 1283, 1180, 1035; HRMS (ES+) m/z calcd. for $C_{11}H_{14}NO_3$ $[M+H]^+$ 208.0974, found 208.0972.

4-Methyl-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione **(13).** The **General Spirocyclization Procedure** was followed at 80 ºC using amide substrate **16** (46 mg, 0.2 mmol). Upon consumption of the starting material, as determined by GC-MS, the reaction mixture was concentrated onto Celite via rotary evaporation and chromatographed by automated flash column chromatography on silica gel eluting with a gradient of 20-80% EtOAc/Hex to afford **13** (30.5 mg, 87%) as a white amorphous solid. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 8.57 (s, 1H), 6.64 (dd, J = 11.1 Hz, J = 3.0 Hz, 2H), 6.35 (dd, J = 11.1 Hz, J = 3.0 Hz, 2H), 6.10 (t, J = 1.5 Hz, 1H), 1.73 (d, J = 1.2 Hz, 3H); 13C{1H} NMR (DMSO-d_6, 75 MHz) δ 184.5, 172.5, 157.7, 148.2, 130.1, 125.4, 64.7, 11.8; FT-IR (cm^{-1}) 3400, 3038, 1704, 1668, 1624, 1278, 1178; HRMS (ES+) m/z calcd. for $C_{10}H_{10}NO_2$ $[M+H]^+$ 176.0712, found 176.0720.

N-(4-(tert-butoxy)phenyl)-3-oxobutanamide **(17).** A modification of the **General Spirocyclization Procedure** was followed. Into a 4 mL vial was added AgOTf (2.6 mg, 5 mol %), $Au(PPh_3)Cl$ (4.9 mg, 5 mol %), a Teflon coated micro stir bar, DCE (2 mL, 0.1M), and water (3.6 uL, 0.2 mmol, 1 equiv.). The mixture was stirred vigorously at room temperature for 2 minutes, after which the amide substrate **16** (46 mg, 0.2 mmol) was added. Upon consumption of the starting material the reaction was concentrated onto Celite and purified via automated flash column chromatography on silica gel eluting with a gradient of 0-50% EtOAc/Hex to afford **17** (41 mg, 82%) as an amorphous white solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.10 (bs, 1H), 7.43 (d, J = 8.7 Hz, 2H), 6.94 (d, J = 9.0 Hz, 2H), 3.56 (s, 2H), 2.30 (s, 3H), 1.32 (s, 9H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 205.2, 163.6, 152.0, 133.2, 124.8, 121.0, 78.7, 50.0, 31.2, 28.8; FT-IR (cm^{-1}) 3304, 3195, 3127, 2976, 2932, 1721, 1664, 1545, 1509, 1163; HRMS (ES+) *m/z* calcd. for $C_{14}H_{20}NO_3$ $[M+H]^+$ 250.1443, found 250.1454.

1-Azaspiro[4.5]deca-3,6,9-triene-2,8-dione **(20a).** The **General Spirocyclization Procedure** was followed at 80 ºC using amide substrate **19a** (65 mg, 0.3 mmol). Upon consumption of the starting material, as determined by GC-MS, the reaction mixture was concentrated onto Celite via rotary evaporation and chromatographed by automated flash column chromatography on silica gel eluting with a gradient of 20-70% EtOAc/Hex to afford **20a** (20 mg, 41%) as a white amorphous solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.34 (bs, 1H), 6.73 (d, J = 4.8 Hz, 1H), 6.54 (d, J = 9.9 Hz, 2H), 6.38 (d, J = 9.9 Hz, 2H), 6.33 (d, J = 5.1 Hz, 1H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 184.2, 173.7, 148.1, 145.1, 131.0, 129.7, 63.1; FT-IR (cm^{-1}) 3924, 3091, 1710, 1661, 1619, 1400, 1330, 1176; HRMS (ES+) *m/z* calcd. for $C_9H_8NO_2$ $[M+H]^+$ 162.0555, found 162.0552.

4-Phenyl-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione **(20b).** The **General Spirocyclization Procedure** was followed at 80 ºC using amide substrate **19b** (58 mg, 0.2 mmol). Upon consumption of the starting material, as determined by GC-MS, the reaction mixture was concentrated onto Celite via rotary evaporation and chromatographed by automated flash column chromatography on silica gel eluting with a gradient of 20-70%

EtOAc/Hex to afford **20a** (30 mg, 64%) as a white amorphous solid. NMR analysis of the product matched the known literature data.[3k]

4-Cyclopropyl-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione **(20c).** The **General Spirocyclization Procedure** was followed at 80 ºC using amide substrate **19c** (52 mg, 0.2 mmol). Upon consumption of the starting material, as determined by GC-MS, the reaction mixture was concentrated onto Celite via rotary evaporation and chromatographed by automated flash column chromatography on silica gel eluting with a gradient of 20-80% EtOAc/Hex to afford **20c** (15 mg, 37%) as a white amorphous solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.56 (d, J = 9.9 Hz, 2H), 6.44 (d, J = 10.2 Hz, 2H), 6.15 (bs, 1H), 5.65 (t, J = 0.9 Hz, 1H), 1.19-1.12 (m, 1H), 1.07-1.01 (m, 2H), 0.74-0.69 (m, 2H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 184.7, 173.9, 167.6, 146.2, 131.4, 117.5, 65.4, 11.7, 8.4; FT-IR (cm^{-1}) 3103, 3057, 2918, 1785, 1645, 1609, 1388, 1280, 1199; HRMS (ES+) *m/z* calcd. for $C_{12}H_{12}NO_2$ $[M+H]^+$ 202.0868, found 202.0873.

4-Cyclohexyl-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione **(20d).** The **General Spirocyclization Procedure** was followed at 80 ºC using amide substrate **19d** (60 mg, 0.2 mmol). Upon consumption of the starting material, as determined by GC-MS, the reaction mixture was concentrated onto Celite via rotary evaporation and chromatographed by automated flash column chromatography on silica gel eluting with a gradient of 30-80% EtOAc/Hex to afford **20d** (28 mg, 57%) as a white amorphous solid. ^{1}H NMR (MeOD-d_4, 300 MHz) δ 6.67 (d, J = 9.9 Hz, 2H), 6.43 (d, J = 9.9 Hz, 2H), 6.15 (s, 1H), 1.84-1.70 (m, 6H), 1.38-1.25 (m, 7H); 13C{1H} NMR (MeOD-d_4, 75 MHz) δ 185.2, 174.7, 169.2, 146.7, 130.5, 122.8, 65.6, 36.4, 33.4, 25.8, 25.2; FT-IR (cm^{-1}) 3098, 2928, 2856, 1696, 1669, 1383, 1348; HRMS (ES+) *m/z* calcd. for $C_{15}H_{18}NO_2$ $[M+H]^+$ 244.1338, found 244.1347.

7-Methyl-4-fluoro-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione **(20e).** The **General Spirocyclization Procedure** was followed at 80 ºC using amide substrate **19e** (50 mg, 0.2 mmol). Upon consumption of the starting material, as determined by GC-MS, the reaction mixture was concentrated onto Celite via rotary evaporation and chromatographed by automated flash column chromatography on silica gel eluting with a gradient of 30-80% EtOAc/Hex to afford **20e** (27 mg, 70%) as a beige amorphous solid. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 8.53 (bs, 1H), 6.71 (dd, J = 9.9 Hz, J = 2.4 Hz, 1H), 6.54 (dd, J = 12.9 Hz, J = 2.4 Hz, 1H), 6.43 (dd, J = 9.9 Hz, J = 7.2 Hz, 1H), 6.12 (s, 1H), 1.78 (s, 3 H); 13C{1H} NMR (DMSO-d_6, 75 MHz) δ 177.6 (d, J = 21.7 Hz), 172.1, 157.6, 153.7 (d, J = 262.9 Hz), 150.0 (d, J = 2.4 Hz), 129.2 (d, J = 3.9 Hz), 125.4, 124.1 (d, J = 12.9 Hz), 65.8 (d, J = 8.6 Hz), 12.0; FT-IR (cm^{-1}) 3265, 3097, 3048, 1658, 1659, 1392, 1168; HRMS (ES+) m/z calcd. for $C_{10}H_9FNO_2$ $[M+H]^+$ 194.0617, found 194.0620.

4-Methyl-7-(trifluoromethyl)-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione **(20f).** The **General Spirocyclization Procedure** was followed at 80 ºC using amide substrate **19f** (49 mg, 0.2 mmol). Upon consumption of the starting material, as determined by GC-MS, the reaction mixture was concentrated onto Celite via rotary evaporation and chromatographed by automated flash column chromatography on silica gel eluting with a gradient of 30-80% EtOAc/Hex to afford **20f** (38 mg, 78%) as a white amorphous solid. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 8.62 (bs, 1H), 7.42 (s, 1H) 6.81 (d, J = 8.1 Hz, 1H), 6.48 (d, J = 9.0 Hz, 1H) 6.22 (s, 1H), 1.75 (s, 3H); 13C{1H} NMR (DMSO-d_6, 75 MHz) δ 179.4, 172.3, 156.4, 151.5 (d, J = 5.1 Hz), 148.7, 129.9, 129.1 (d, J = 29.2 Hz) 126.6, 121.4 (quart. J = 271.9 Hz), 64.2, 12.0; FT-IR (cm^{-1}) 3276, 3107, 3040, 1685, 1656, 1392, 1293, 1152, 1032; HRMS (ES+) m/z calcd. for $C_{11}H_9F_3NO_2$ $[M+H]^+$ 244.0585, found 244.0573.

4,7-Dimethyl-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione **(20g).** The **General Spirocyclization Procedure** was followed at 80 ºC using amide substrate **19g** (49 mg, 0.2 mmol). Upon consumption of the starting material, as determined by GC-MS, the reaction mixture was concentrated onto Celite via rotary evaporation and

chromatographed by automated flash column chromatography on silica gel eluting with a gradient of 30-80% EtOAc/Hex to afford **20g** (28 mg, 74%) as a beige amorphous solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.61 (bs, 1H), 6.47 (dd, J = 9.9 Hz, J = 2.7 Hz, 1H), 6.41 (d, J = 9.9 Hz, 1H) 6.26 (quart., J = 1.2 Hz, 1H), 6.03 (quart, J = 1.5 Hz, 1H), 1.94 (d, J = 1.2 Hz, 3H), 1.82 (d, J = 1.2 Hz, 3H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 185.3, 174.0, 159.6, 145.9, 140.9, 138.5, 131.3, 124.8, 65.8, 15.9, 12.5; FT-IR (cm^{-1}) 3207, 3101, 2920, 1667, 1398, 1330, 1121; HRMS (ES+) *m/z* calcd. for $C_{11}H_{12}NO_2$ $[M+H]^+$ 190.0868, found 190.0872.

6-Methoxy-4-methyl-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione **(20h).** The **General Spirocyclization Procedure** was followed at 80 ºC using amide substrate **19h** (53 mg, 0.2 mmol). Upon consumption of the starting material, as determined by GC-MS, the reaction mixture was concentrated onto Celite via rotary evaporation and chromatographed by automated flash column chromatography on silica gel eluting with a gradient of 30-90% EtOAc/Hex to afford **20h** (35 mg, 85%) as a white amorphous solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.81 (bs, 1H), 6.34 (d, J = 8.4 Hz, 1H), 6.14 (d, J = 9.9 Hz, 1H), 5.95 (s, 1H), 5.62 (s, 1H), 3.84 (s, 3H), 1.81 (s, 3H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 193.6, 175.6, 171.8, 158.5, 140.0, 125.1, 124.2, 100.2, 71.9, 56.4, 12.4; FT-IR (cm^{-1}) 3173, 3056, 1694, 1655, 1571, 1388, 1228, 1168; HRMS (ES+) *m/z* calcd. for $C_{11}H_{12}NO_3$ $[M+H]^+$ 206.0817, found 206.0820.

Spirolactam **22a.** The **General Spirocyclization Procedure** was followed at 80 ºC using amide substrate **21a** (84 mg, 0.2 mmol). Upon consumption of the starting material, as determined by GC-MS, the reaction mixture was concentrated onto Celite via rotary evaporation and chromatographed by automated flash column chromatography on silica gel eluting with a gradient of 30-80% EtOAc/Hex to afford **22a** (55 mg, 76%) as a white amorphous solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.36-7.30 (m, 5H, partially eclipsed by residual solvent peak), 6.61 (d, J = 9.3 Hz, 1H), 6.41 (d, J = 9.0 Hz, 1H), 6.33 (d, J = 9.6 Hz, 1H), 6.20-6.16 (apparent d due to overlapping peaks, 2H), 5.78 (bs, 1H), 4.97 (bs, 1H), 1.78 (s, 3H), 1.30 (s, 9H); 13C{1H} NMR ($CDCl_3$, 75

MHz) δ 184.5, 168.2, 156.4, 146.0, 135.2, 131.7, 131.4, 129.3, 129.1, 128.8, 125.5, 70.0, 62.4, 51.7, 28.5, 12.5; FT-IR (cm^{-1}) 3515, 3325, 3067, 3008, 2968, 1966, 1887, 1815, 1677, 1629, 1542, 1455, 1387, 1340, 1229; HRMS (ES+) *m/z* calcd. for $C_{22}H_{25}N_2O_3$ $[M+H]^+$ 365.1865, found 365.1851.

Spirolactam **22b.** The **General Spirocyclization Procedure** was followed at 80 ºC using amide substrate **21b** (136 mg, 0.28 mmol). Upon consumption of the starting material, as determined by GC-MS, the reaction mixture was concentrated onto Celite via rotary evaporation and chromatographed by automated flash column chromatography on silica gel eluting with a gradient of 30-80% EtOAc/Hex to afford **22b** (76 mg, 65%) as a white amorphous solid. ^1H NMR ($CDCl_3$, 300 MHz) δ 7.35 (d, *J* = 7.5 Hz, 1H), 7.30-7.25 (m, 1H partially eclipsed by residual solvent peak), 7.22-7.15 (m, 3H), 6.51 (dd, *J* = 9.9 Hz, *J* = 1.8 Hz, 1H), 6.41 (dd, *J* = 9.9 Hz, *J* = 1.5 Hz, 1H), 6.36 (dd, *J* = 9.9 Hz, *J* = 3.0 Hz, 1H), 6.28 (dd, *J* = 10.2 Hz, *J* = 3.0 Hz, 1H), 6.12 (s, 1H), 3.71 (bm, 1H), 3.68 (t, *J* = 8.4 Hz, 1H), 2.61 (t, *J* = 7.5 Hz, 2H), 2.57-2.48 (m, 1H), 2.33-2.26 (m, 1H), 1.87-1.81 (m, 2H eclipsed by methyl singlet at 1.81), 1.81 (s, 3H), 1.71-1.67 (m, 2H partially eclipsed by water), 1.48-1.39 (m, 2H), 1.38-1.21 (m, 4H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 183.9, 172.6, 157.0, 144.9, 144.1, 140.5, 133.4, 133.3, 128.7, 128.6, 126.4, 126.0, 70.9, 60.7, 48.1, 33.0, 32.8, 32.1, 25.6, 24.7, 24.6, 12.9; FT-IR (cm^{-1}) 3304, 3061, 2930, 2857, 1675, 1539, 1363; HRMS (ES+) *m/z* calcd. for $C_{26}H_{31}N_2O_3$ $[M+H]^+$ 419.2335, found 419.2340.

Spirolactam **22c.** The **General Spirocyclization Procedure** was followed at 80 ºC using amide substrate **21c** (75 mg, 0.17 mmol). Upon consumption of the starting material, as determined by GC-MS, the reaction mixture was concentrated onto Celite via rotary evaporation and chromatographed by automated flash column chromatography on silica gel eluting with a gradient of 30-80% EtOAc/Hex to afford **22c** (45 mg, 68%) as a white amorphous solid. ^1H NMR ($CDCl_3$, 300 MHz) δ 7.39-7.29 (m, 5H), 6.62 (d, *J* = 9.6 Hz, 1H), 6.42 (d, *J* = 9.3 Hz, 1H), 6.34 (d, *J* = 9.9 Hz, 1H), 6.18 (apparent doublet due to overlapping peaks, 2H), 5.87 (d, *J* = 4.5 Hz,

1H), 5.02 (s, 1H), 3.78 (bs, 1H), 2.00-1.86 (m, 2H), 1.79 (s, 3H), 1.64-1.54 (m, 3H), 1.38-1.26 (m, 2H), 1.16-1.01 (m, 3H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 184.5, 171.1, 167.9, 156.5, 146.0, 135.1, 131.9, 131.5, 129.4, 129.1, 128.8, 125.5, 70.1, 61.9, 48.9, 32.7, 32.6, 25.5, 24.7, 24.6, 12.6; FT-IR (cm^{-1}) 3429, 3034, 2930, 2853, 1665, 1561, 1342; HRMS (ES+) *m/z* calcd. for $C_{24}H_{27}N_2O_3$ $[M+H]^+$ 391.2022, found 391.2005.

1,4-Dimethyl-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione **(24a).** The **General Spirocyclization Procedure** was followed at 50 ºC using amide substrate **23a** (38 mg, 0.2 mmol). Upon consumption of the starting material, as determined by GC-MS, the reaction mixture was concentrated onto Celite via rotary evaporation and chromatographed by automated flash column chromatography on silica gel eluting with a gradient of 30-80% EtOAc/Hex to afford **24a** (29 mg, 77%) as a white amorphous solid. ^1H NMR ($CDCl_3$, 300 MHz) δ 6.56 (d, J = 10.2 Hz, 2 H), 6.39 (d, J = 10.2 Hz, 2 H), 6.14 (d, J = 1.5 Hz, 2H), 2.85 (s, 3H), 1.85 (d, J = 1.5 Hz, 3H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 184.1, 170.8, 155.2, 145.8, 133.2, 125.6, 69.0, 26.1, 12.6; FT-IR (cm^{-1}) 3358, 3065, 2940, 1669, 1388, 1361, 1060; HRMS (ES+) *m/z* calcd. for $C_{11}H_{12}NO_2$ $[M+H]^+$ 190.0868, found 190.0877.

7-Chloro-4-methyl-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione **(24b).** The **General Spirocyclization Procedure** was followed at 50 ºC using amide substrate **23b** (42 mg, 0.2 mmol). Upon consumption of the starting material, as determined by GC-MS, the reaction mixture was concentrated onto Celite via rotary evaporation and chromatographed by automated flash column chromatography on silica gel eluting with a gradient of 30-80% EtOAc/Hex to afford **24b** (32 mg, 76%) as a white amorphous solid. ^1H NMR ($CDCl_3$, 300 MHz) δ 7.33 (s, 1H), 6.68 (s, 1H), 6.53 (d, J = 1.2 Hz, 1H), 6.10 (d, J = 1.2 Hz, 1H), 1.88 (s, 3H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 177.7, 173.3, 158.4, 146.4, 141.7, 135.1, 130.6, 125.7, 66.8, 12.7; FT-IR (cm^{-1}) 3291, 3094, 3038, 1665, 1385, 1323, 1022; HRMS (ES+) *m/z* calcd. for $C_{10}H_9ClNO_2$ $[M+H]^+$ 210.0322, found 210.0325.

7-Methoxy-4-methyl-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione **(24c).** The **General Spirocyclization Procedure** was followed at 50 ºC using amide substrate **23c** (41 mg, 0.2 mmol). Upon consumption of the starting material, as determined by GC-MS, the reaction mixture was concentrated onto Celite via rotary evaporation and chromatographed by automated flash column chromatography on silica gel eluting with a gradient of 30-100% EtOAc/Hex to afford **24c** (34.5 mg, 84%) as a white amorphous solid. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 8.43 (s, 1H), 6.61 (d, J = 9.0 Hz, 1H), 6.33 (d, J = 9.3 Hz, 1H), 6.04 (s, 1H), 5.61 (s, 1H), 3.57 (s, 3H), 1.74 (s, 3H); 13C{1H} NMR (DMSO-d_6, 75 MHz) δ 179.7, 172.2, 159.2, 151.7, 148.7, 129.6, 124.5, 114.7, 65.8, 55.0, 11.9; FT-IR (cm^{-1}) 3202, 3057, 2945, 1665, 1637, 1389, 1206, 1113, 1019; HRMS (ES+) *m/z* calcd. for $C_{11}H_{12}NO_3$ $[M+H]^+$ 206.0817, found 206.0810.

4,6-Dimethyl-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione **(24d).** The **General Spirocyclization Procedure** was followed at 50 ºC using amide substrate **23d** (38 mg, 0.2 mmol). Upon consumption of the starting material, as determined by GC-MS, the reaction mixture was concentrated onto Celite via rotary evaporation and chromatographed by automated flash column chromatography on silica gel eluting with a gradient of 30-80% EtOAc/Hex to afford **24d** (32 mg, 84%) as a white amorphous solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.45 (d, J = 9.9 Hz, 1H), 6.41 (dd, J = 9.9 Hz, J = 1.5 Hz, 1H), 6.33 (s, 1H), 6.12 (s, 1H), 1.80 (d, J = 1.2 Hz, 3H), 1.76 (d, J = 1.2 Hz, 3H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 185.2, 174.5, 159.8, 154.8, 146.3, 131.0, 130.1, 125.5, 67.7, 17.4, 12.2; FT-IR (cm^{-1}) 3244, 2978, 1696, 1389, 1332, 1283; HRMS (ES+) *m/z* calcd. for $C_{11}H_{12}NO_2$ $[M+H]^+$ 190.0868, found 190.0877.

4,7,9-Trimethyl-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione **(24e).** The **General Spirocyclization Procedure** was followed at 50 ºC using amide substrate **23e** (41 mg, 0.2 mmol). Upon consumption of the starting material,

as determined by GC-MS, the reaction mixture was concentrated onto Celite via rotary evaporation and chromatographed by automated flash column chromatography on silica gel eluting with a gradient of 50-75% EtOAc/Hex to afford **24e** (34 mg, 83%) as a white amorphous solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.82 (s, 1H), 6.23 (s, 2H), 6.00 (s, 1H), 1.94 (s, 6H), 1.79 (s, 3H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 186.0, 173.7, 160.2, 140.7, 138.3, 124.4, 65.4, 16.2, 12.6; FT-IR (cm^{-1}) 3356, 2918, 1706, 1627; HRMS (ES+) *m/z* calcd. for $C_{12}H_{14}NO_2$ $[M+H]^+$ 204.1025, found 204.1032.

7,9-Dichloro-4methyl-1-azaspiro[4.5]deca-3,6,9-triene-2,8-dione **(24f).** A modification of the **General Spirocyclization Procedure** was followed. The reaction was stirred at 80 ºC employing 10 mol % of both $Au(PPh_3)Cl$ and AgOTf, using amide substrate **23f** (49 mg, 0.2 mmol). Aliquots were removed every 30 minutes and analyzed by GC-MS. After 5 hours at 80 ºC the reaction was stopped and the reaction mixture was concentrated onto Celite via rotary evaporation and chromatographed by automated flash column chromatography on silica gel eluting with a gradient of 40-80% EtOAc/Hex to afford **24f** (17 mg, 35%) as a white amorphous solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.87 (s, 1H), 6.71 (s, 2H), 6.13 (s, 1H), 1.91 (s, 3H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 172.6, 172.1, 157.8, 142.0, 134.3, 125.9, 66.8, 12.9; FT-IR (cm^{-1}) 3340, 3044, 1679, 1598, 1391, 1315, 1050; HRMS (ES+) *m/z* calcd. for $C_{10}H_8Cl_2NO_2$ $[M+H]^+$ 243.9932, found 243.9940.

3'-Methyl-4H-spiro[naphthalene-1,2'-pyrrole]-4,5'(1H)-dione **(26).** The **General Spirocyclization Procedure** was followed at 50 ºC using amide substrate **25** (45 mg, 0.2 mmol). Upon consumption of the starting material, as determined by GC-MS, the reaction mixture was concentrated onto Celite via rotary evaporation and chromatographed by automated flash column chromatography on silica gel eluting with a gradient of 30-80% EtOAc/Hex to afford **26** (38.5 mg, 85%) as a white amorphous solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.17 (dd, J = 8.1 Hz, J = 1.5 Hz, 1 H), 7.59 (dt, J = 7.5 Hz, J = 1.5 Hz, 1H), 7.49 (dt, J = 7.5 Hz, J = 1.2 Hz, 1H), 7.29-7.26

(m, 1H, eclipsed by residual solvent peak), 6.83 (bs, 1H), 6.61 (apparent d, 2H), 6.04 (d, J = 1.5 Hz, 1H), 1.60 (d, J = 1.5 Hz, 3H); 13C{1H} NMR ($CDCl_3$, 75 MHz) δ 183.7, 174.2, 162.6, 146.6, 138.9, 133.8, 131.5, 131.4, 129.2, 127.4, 126.0, 123.5, 65.8, 12.5; FT-IR (cm^{-1}) 3244, 3071, 1697, 1666, 1599, 1381, 1299, 1153; HRMS (ES+) m/z calcd. for $C_{14}H_{12}NO_2$ $[M+H]^+$ 226.0868, found 226.0869.

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Notes

The authors declare no competing financial interest.

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ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at http://pubs.acs.org.

^{1}H and ^{13}C NMR spectra

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