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### ARTICLE

## Electrophilic Activation of Alkynes. Aimee K. Clarke, John T. R. Liddon, James D. Cuthbertson, Richard J. K. Taylor\* and William P.

with much greater efficiency. Initial asymmetric studies are also outlined.

Received 00th January 20xx, Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

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Two complementary dearomatising spirocyclisation protocols to generate spirocyclic dienones from anisole and phenoltethered ynones are described, each proceeding via electrophilic alkyne activation. The first approach focuses on the spirocyclisation of *para*-substituted anisoles using either SnCl<sub>2</sub>·2H<sub>2</sub>O or Cu(OTf)<sub>2</sub>. The second approach, which enables the spirocyclisation of both *ortho*- and *para*-substituted phenols, uses silica-supported AgNO<sub>3</sub> to generate similar scaffolds

Dearomatisation Approaches to Spirocyclic Dienones via the

#### Introduction

Spirocyclic dienones are key structural features in numerous bioactive natural products isolated from a variety of trees, plants and bacteria, with representative examples 1-6 shown in Figure 1.<sup>1a-e</sup>

Unsworth\*



Figure 1. Natural products containing spirocyclic dienone motifs.

A popular approach to synthesise spirocyclic dienones is via the dearomatisation and *ipso*-cyclisation of a phenol or anisole derivative, with this typically achieved using one of two methods (Scheme 1). The most common method is based on the oxidation of a substituted phenol (Scheme 1a); following oxidation of the phenol, an intramolecular nucleophilic *ipso*-

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Electronic Supplementary Information (ESI) available: optimisation table and NMR spectra. See DOI: 10.1039/x0xx00000x

cyclisation reaction can take place with a range of Cnucleophiles including alkenes/alkynes,<sup>2a</sup> enamides,<sup>2b</sup> allyl silanes,<sup>2c,d</sup> enols/enolates,<sup>2e</sup> aromatics,<sup>2f</sup> nitro compounds<sup>2g</sup> and diazo compounds.<sup>2h,i</sup> Alternatively, the flow of electron density can be reversed and a substituted phenol/anisole can react directly with a tethered electrophilic species (Scheme 1b); examples of electrophilic *ipso*-cyclisation with sulfonates,<sup>3a-c</sup> nitriles,<sup>3d</sup> epoxides,<sup>3e</sup> activated allenes,<sup>3f</sup> activated aryl halides,<sup>3g</sup> propargyl bromides/carbonates,<sup>3h</sup> activated alkynes/alkenes<sup>3i-k</sup> and allylic carbonates<sup>3I,m</sup> have all been reported.



Scheme 1. General methods for spirocyclic dienone synthesis.

In this manuscript, two complementary protocols which generate spirocyclic dienones are outlined (Scheme 1c), with both methods promoted by the activation of a tethered alkyne moiety.<sup>4</sup> The first approach focuses on the spirocyclisation of

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*para*-substituted anisoles using either  $SnCl_2 \cdot 2H_2O$  or  $Cu(OTf)_2$  to activate the alkyne towards nucleophilic attack, while the second uses silica-supported AgNO<sub>3</sub> to generate similar scaffolds from analogous phenol precursors with greater efficiency and scope. Substrate scoping studies are described for each reaction series, while comparisons between the two reaction types, synthetic extensions and preliminary asymmetric results are also outlined.

#### **Results and discussion**

This research program began during a project to synthesise the spirocyclic natural product spirobacillene A (**6**, Figure 1).<sup>5,6</sup> In this published work, it was found that treating anisole-tethered ynone **7** with five equivalents of  $SnCl_2 \cdot 2H_2O^7$  at RT in  $CH_2Cl_2$  resulted in its efficient conversion into spirocyclic dienone **8**, which was isolated in 89% yield (Scheme 2). The ease and scalability of this key step was instrumental in allowing us to complete the synthesis of spirobacillene A **6**, which was published in 2013.<sup>5,8</sup>



Scheme 2. Sn(II)-mediated synthesis of spirobacillene A.

This initial discovery inspired the development of a number of other classes of dearomatising spirocyclisation reactions<sup>9</sup> in our group in the following years.<sup>10,11</sup> However, prior to this publication, the conversion of ynone **7** into spirocycle **8** remained the only reported reaction of its type in the literature,<sup>12</sup> hence it was decided to further optimise this process and to evaluate its scope.

Initial results were disappointing, with unsubstituted and alkyl substituted ynones 9a and 9b both failing to react with  $SnCl_2 \cdot 2H_2O$  under the conditions used during the total synthesis of spirobacillene A (Table 1, entries 1 and 2). Phenyl substituted ynone 9c also failed to react at room temperature (entry 3), although a small amount of cyclisation was observed upon heating at reflux (entry 4). A plausible explanation for this poor reactivity is that the more electron-rich the alkyne, the more readily it can interact with acidic additives, promoting spirocyclisation. Support for this theory was found when examining the cyclisation of anisole-substituted ynone 9d; under the standard SnCl<sub>2</sub>·2H<sub>2</sub>O mediated conditions, a more respectable 75% conversion into spirocyclic dienone 10d was observed (entry 5, 57% isolated yield). Pleasingly, the spirocyclisation was improved significantly by changing the catalyst; full details of reaction optimisation are included in the Supplementary Information, with the highlight being the discovery that Cu(OTf)<sub>2</sub> promoted the complete cyclisation of ynone 9d within 1 h, with spirocycle 10d isolated in 80% isolated yield (entry 6). However, Cu(OTf)<sub>2</sub> did not lead to any

improvement in the reactivity of substrates **9a–9c**, forcing us to concede that an electron donating group on the alkyne terminus is a requirement for this transformation.





Entry	Ynone	Reagent	Equiv/ Time [h]/ Temp [°C]	Conversion <sup>[a],[b]</sup> (isolated yield in brackets)
1	9a	SnCl₂·2H₂O	5/20/RT or 45	No Reaction
2	9b	SnCl <sub>2</sub> ·2H <sub>2</sub> O	5/20/RT or 45	No Reaction
3	9c	SnCl <sub>2</sub> ·2H <sub>2</sub> O	5/20/RT	No Reaction
4	9c	SnCl <sub>2</sub> ·2H <sub>2</sub> O	5/20/45	10%
5	9d	SnCl₂·2H₂O	5/20/RT	75% (57%)
6	9d	Cu(OTf) <sub>2</sub>	1/1/RT	>95% (80%)
[a] All reactions were performed using $0.09-0.20$ mmol of the vnone <b>9a-d</b> in CH <sub>2</sub> Cl <sub>2</sub> (0.1				

[a] All reactions were performed using 0.09–0.20 mmol of the ynone 9a-d in CH<sub>2</sub>Cl<sub>2</sub> (0.1 M);
 [b] Conversion measured by analysis of the <sup>1</sup>H NMR spectra of the unpurified reaction mixture.

With this in mind, a series of anisoles tethered to electron-rich vnones (9d-I) were made and tested using both SnCl<sub>2</sub>·2H<sub>2</sub>O and Cu(OTf)<sub>2</sub> to activate the alkyne (Table 2). Spirocycle 10e was formed in just 1 h from aniline-substituted ynone 9e using one equivalent of SnCl<sub>2</sub>·2H<sub>2</sub>O. Alternatively, the same product could be made using catalytic  $Cu(OTf)_2$  (0.1 equivalents), albeit with a longer reaction time. Thiophene-substituted ynone 9f reacted more slowly; the cyclisation was incomplete following treatment with SnCl<sub>2</sub>·2H<sub>2</sub>O at room temperature for 3 days, but proceeded more efficiently with Cu(OTf)<sub>2</sub> to afford **10f** in a 73% yield. Substitution around either ring system is well tolerated, evidenced by the efficient syntheses of compounds 10g-i. Vinyl sulfide product 10j could also be isolated in a reasonable yield using Cu(OTf)2, demonstrating compatibility with non-aromatic-tethered ynones. Additionally, the reaction is not limited to the synthesis of spirocyclic cyclopentenones; spirocyclic cyclohexenones 10k and 10l were both formed in good yields, although the reactions were slower and thus required additional heating or a longer reaction time.

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Table 2. Substrate scope of spirocyclisation of anisole-tethered ynones using

[a] All reactions were performed in CH<sub>2</sub>Cl<sub>2</sub> (0.1 M) at RT with 1 equiv. of reagent unless specified. Where stated, reaction conversions were measured by analysis of the <sup>1</sup>H NMR spectra of the unpurified reaction mixture; [b] 5 equiv. of SnCl<sub>2</sub>·2H<sub>2</sub>O used; [c] 0.1 equiv. of Cu(OTf)<sub>2</sub> used; [d] Reaction performed at 50 °C.

To summarise this reaction series, *para*-substituted anisoles tethered to electron-rich ynones can be converted into spirocyclic dienones in high yield using either a Sn(II) or Cu(II) reagent. The simplicity of the synthetic procedure and mild reaction conditions are the most pleasing aspects of this method, although the use of relatively large quantities of Sn(II) and Cu(II) reagents and the requirement to use electron-rich ynones were both identified as areas with potential for improvement.

It was reasoned that both of the above limitations might be addressed by using a more active catalyst. Silver(I) catalysts were identified as particularly promising candidates, given that they have generally been found to be the best catalyst class in related alkyne activation processes,<sup>10</sup> but disappointingly, the Ag(I) catalysts tested were ineffective for the spirocyclisation of anisole system **9d**. However, by switching the nucleophilic component in the starting material from an anisole to the analogous phenol, the desired spirocyclic product **10d** could indeed be formed, and with Ag(I) catalysts now viable for this transformation, significant improvements in the scope and efficiency soon emerged. The use of silica-supported AgNO<sub>3</sub> (10 mol%) in CH<sub>2</sub>Cl<sub>2</sub> at RT was found to be a particularly active and convenient catalyst system and was chosen for the substrate scoping studies, which were performed on ynone tethered phenols (**11c**,**d**,**m**–**v**). For clarity, five of these examples (denoted in the table with a \*) were included in an earlier publication,<sup>10c</sup> while the other seven substrates are novel examples (Table 3). It should also be noted that AgNO<sub>3</sub>·SiO<sub>2</sub> is a much more reactive catalyst than unsupported AgNO<sub>3</sub>; ynones **11c**,**d**,**m**,**o**,**q**-**v** did not react in the presence of unsupported AgNO<sub>3</sub> and only a 7% conversion to spirocyclic dienone **10n** was observed for ynone **11n** when using unsupported AgNO<sub>3</sub>.<sup>13</sup>

DOI: 10.1039/C6OB02426B

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Table 3. Substrate scope of AgNO<sub>3</sub>·SiO<sub>2</sub>-catalysed dearomatisation/spirocyclisations.



[a] All reactions were performed using 1 wt. % AgNO<sub>3</sub>·SiO<sub>2</sub> in CH<sub>2</sub>Cl<sub>2</sub> (0.1 M) at RT unless specified otherwise; [b] Reaction performed at 40 °C. Compounds highlighted with a \* were featured in our earlier publication (see reference 10c); all other examples are novel.

It quickly became apparent that by changing the catalyst and starting material, the requirement for an electron-donating substituent on the ynone had been removed; simple alkyl chains and aromatic substituents in the R<sup>1</sup> position were all well tolerated, generating spirocyclic dienone products 10c, 10d, 10n in high yields. Alkyl substituted ynones bearing protected amine and alcohol groups (11o and 11p) also reacted smoothly to furnish their corresponding spirocyclic dienones (10o and 10p). The incorporation of terminal cyclopropane and cyclopentane rings appeared to increase the reactivity of the ynone; dienones 10q and 10r were produced in near-quantitative yields in 2-6 h which is notably faster than most of the other reactions explored in this study. Pleasingly, we were also able to perform the spirocyclisation on orthosubstituted phenols 11s-v; there are relatively few literature examples of dearomatisation and ipso-cyclisation reactions of ortho-substituted phenols, and so the efficient syntheses of chiral spirocyclic products 12s-v in 90-99% yields are especially pleasing.<sup>2d,14</sup>

The superior reactivity of the Ag(I) mediated reaction system compared to the earlier Sn(II)/Cu(II) reactions is best demonstrated by a direct comparison. Thus, our published synthesis of spirocyclic dienone **8**, which is a key intermediate en route to spirobacillene A, required five equivalents of SnCl<sub>2</sub>·2H<sub>2</sub>O and 18 h to generate the product in 89% yield.<sup>5</sup> In contrast, the same product was generated from phenol **13** in near-quantitative yield in just 7 h using 10 mol% AgNO<sub>3</sub>·SiO<sub>2</sub> (Scheme 3).



Scheme 3. Previous and improved routes to spirobacillene A precursor 8.

The potential of the spirocyclic dienone products to undergo additional complexity generating reactions has also been briefly demostrated; spirocyclic products **10o** and **10p** were each found to undergo protecting group cleavage and cyclisation in one-pot to furnish novel tricyclic products **14** and **15** as single diastereomers and in reasonable, unoptimised yields (Scheme 4).



Scheme 4. One-pot deprotection and cyclisation of spirocyclic dienones  ${f 10o}$  and  ${f 10p}.$ 

Finally, having shown that *ortho*-substituted phenols can be converted into chiral spirocyclic dienones, the possibility of performing this reaction asymmetrically has also been briefly examined. Preliminary studies show that spirocyclisation can be achieved with a modest amount of asymmetric induction (23% *ee*) using the BINOL-based chiral phosphoric acid silver(I) salt **16** (Scheme 5). It is envisaged that optimisation of the reaction conditions and the nature of the silver(I) catalyst<sup>15</sup> should lead to improve enatioselectivity in this process.



Scheme 5. Asymmetric spirocyclisation reaction using silver salt of CPA 16.

#### Conclusions

In summary, two mild and efficient methods for the synthesis of spirocyclic dienones are described. Both were briefly introduced by our group in previous publications, but the significantly expanded substrate scoping studies outlined in this manuscript mean that each can now be considered as general and versatile synthetic approach to this important compound class. Both methods work well on a variety of easy-to-synthesise ynone precursors. The use of catalytic AgNO<sub>3</sub>·SiO<sub>2</sub> to promote the spirocyclisation of ynone tethered phenols is likely to be of particular interest, in view of the excellent isolated yields in this series, the simple product purification and the capacity to recover the active catalyst by filtration.

#### Experimental

Except where stated, all reagents were purchased from commercial sources and used without further purification.  $^1\mathrm{H}$ 

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NMR and <sup>13</sup>C NMR spectra were recorded on a JEOL ECX400 or JEOL ECS400 spectrometer, operating at 400 MHz and 100 MHz respectively. All spectral data were acquired at 295 K. Chemical shifts ( $\delta$ ) are quoted in parts per million (ppm). The residual solvent peak,  $\delta_{\rm H}$  7.26 and  $\delta_{\rm C}$  77.0 for CDCl\_3 and  $\delta_{\rm H}$  2.50 and  $\delta_{c}$  39.5 for DMSO- $d_{6}$ . Coupling constants (J) are reported in Hertz (Hz) to the nearest 0.5 Hz. The multiplicity abbreviations used are: s (singlet), d (doublet), t (triplet), g (quartet), m (multiplet), br (broad). Signal assignment was achieved by analysis of DEPT, COSY, NOESY, HMBC and HSQC experiments where required. Infrared (IR) spectra were recorded on a PerkinElmer UATR 2 Spectrometer as a thin film dispersed from either CH<sub>2</sub>Cl<sub>2</sub> or CDCl<sub>3</sub> and are reported in wavenumbers (cm<sup>-1</sup>). Mass-spectra were obtained by the University of York Mass Spectrometry Service, using electrospray ionisation (ESI) on a Bruker Daltonics, Micro-tof spectrometer. Melting points were determined using Gallenkamp apparatus and are uncorrected. Reactions were monitored using thin layer chromatography (TLC), which was carried out on Merck silica gel 60F254 pre-coated aluminium foil sheets and were visualised using UV light (254 nm) and stained with basic aqueous potassium permanganate. Flash column chromatography was carried out using slurry packed Fluka silica gel (SiO<sub>2</sub>), 35–70  $\mu$ m, 60 Å, under a light positive pressure, eluting with the specified solvent system. Compounds **9d**<sup>16</sup> and **9e**<sup>10a</sup> were prepared according to literature procedures.

#### **General Experimental**

#### **General Procedure A: Weinreb Amide Synthesis I**

To a suspension of acid (1.00 mmol) in DCM (2 mL) at RT was added CDI (220 mg, 1.20 mmol). A homogeneous solution quickly formed, and was stirred at RT for 1 h, after which time MeNH(OMe)·HCl (107 mg, 1.10 mmol) and stirring continued for a further 2 h. The crude reaction mixture was then poured into water (10 mL) and basified to *ca.* pH 10 with 2 M aq. NaOH extracted with EtOAc ( $3 \times 30$  mL) and washed with 10% aq. HCl (15 mL). The organic extracts were dried over MgSO<sub>4</sub> and concentrated *in vacuo*, affording the Weinreb amide product which was used without further purification.

#### **General Procdure A2: Weinreb Amide Synthesis II**

To a stirred solution of acid (1.00 mmol), MeNH(OMe)·HCl (107 mg, 1.10 mmol) and DIPEA (0.52 mL, 3.00 mmol) in  $CH_2Cl_2$  (2.5 mL) was added T3P 50% in EtOAc (955 mg, 1.50 mmol). The solution was stirred at RT until completion was observed by TLC. The reaction mixture was poured into water (10 mL) and acidified using 10% aq. HCl (5 mL). The organics were collected and the aqueous extracted with EtOAc (3 × 30 mL). The organics were combined, washed with aq. 2 M NaOH (10 mL), brine (10 mL), dried over MgSO<sub>4</sub> and concentrated *in vacuo* to afford the Weinreb amide product which was used without further purification.

**General Procedure B: Ynone Formation I** 

To a solution of terminal alkyne (1.50 mmol) in THF (10 mL) at -78 °C was added n-BuLi (0.875 mL, 1.4 mmol, 1.6 M in hexanes). The resulting yellow solution was stirred at -78 °C for 30 min, then transferred via cannula to a cooled (-78 °C) solution of Weinreb amide (1.00 mmol) in THF (5 mL). The mixture was stirred at -78 °C for 5 min then warmed to -10 °C and stirred for a further 1 h. The reaction was then re-cooled to -78 °C and quenched with sat. aq. NH<sub>4</sub>Cl (30 mL), allowed to warm to RT, diluted with water (70 mL), extracted with EtOAc (3 × 100 mL), dried over MgSO<sub>4</sub> and concentrated *in vacuo*. Purification by flash column chromatography (10:1 petrol:EtOAc to elute the excess alkyne, then 5:1 petrol:EtOAc to elute the product) afforded the ynone product.

DOI: 10.1039/C6OB02426B

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#### **General Procedure B2: Ynone Formation II**

To a stirred solution of alkyne (3.00 mmol) in THF (3 mL) at -78 °C under argon was added *n*-BuLi (1.00 mL, 2.5 mmol, 2.5 M in hexanes) dropwise. The mixture was stirred for 30 min at -78 °C and then transferred *via* cannula to a -78 °C solution of Weinreb amide (1.00 mmol) in THF (5 mL). Upon complete transfer the mixture was warmed to RT and stirred for the specified amount of time. The reaction was quenched with sat. aq. NH<sub>4</sub>Cl (30 mL), diluted with water (70 mL) and extracted with EtOAc (3 × 100 mL). The organics were combined, washed with brine (100 mL), dried over MgSO<sub>4</sub>, concentrated *in vacuo* and purified by flash column chromatography to afford the ynone product.

#### General Procedure C: Spirocyclisation using Sn(II)/Cu(II)

To a solution of ynone (1.00 mmol) in  $CH_2CI_2$  (10 mL) was added an acid catalyst (0.1–5.0 equiv.). The resulting suspension was stirred at the specified temperature until completion was observed by TLC, before adding an excess of solid K<sub>2</sub>CO<sub>3</sub> and stirring for an additional 10 min. The mixture was then filtered, rinsed with  $CH_2CI_2$  and concentrated *in vacuo*. Purification by flash column chromatography afforded the spirocyclic product.

#### General Procedure C2: Spirocyclisation using AgNO<sub>3</sub>·SiO<sub>2</sub>

To a solution of ynone (1 mmol) in  $CH_2CI_2$  (10 mL) was added  $AgNO_3 \cdot SiO_2$  (0.01–0.1 equiv., 1 wt. %  $AgNO_3$  on  $SiO_2$ ). The mixture was stirred at the specified temperature until completion was observed by TLC. The reaction mixture was filtered, washing the catalyst with EtOAc (10 mL), then concentrated *in vacuo* to afford the spirocyclic product.

#### **Compound Synthesis**

#### 4-(4-Methoxyphenyl)spiro[4.5]deca-3,6,9-triene-2,8-dione

(10d). Synthesised using general procedure C from ynone 9d (25.0 mg, 0.0892 mmol) and copper(II) triflate (32.3 mg, 0.0892 mmol) for 1 h at RT. Purification by flash column chromatography (2:1 petrol:EtOAc) afforded the *title compound* 10d as a brown solid (19 mg, 80%); mp. 135–137 °C; R<sub>f</sub> 0.20 (1:1 petrol:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 1669, 1639, 1579, 1541, 1488, 1234, 1163, 1013, 848, 822;  $\delta_{\rm H}$  (400 MHz, CDCl<sub>3</sub>) 2.75 (2 H, s), 3.81 (3 H, s), 6.46 (2 H, d, *J* = 10.0), 6.62 (1

# DOI: 10.1039/C6OB02426B

H, s), 6.85 (2 H, d, J = 9.0), 6.95 (2 H, d, J = 10.0), 7.48 (2 H, d, J = 9.0);  $\delta_{C}$  (100 MHz, CDCl<sub>3</sub>) 46.8, 51.0, 55.4, 114.3, 125.3, 127.5, 129.4, 130.0, 152.0, 162.3, 173.1, 184.7, 203.0; HRMS (ESI<sup>+</sup>): Found: 289.0825; C<sub>17</sub>H<sub>14</sub>NaO<sub>3</sub> (MH<sup>+</sup>) Requires 289.0835 (3.5 ppm error). Spectroscopic data matched those previously reported in the literature.<sup>16</sup>

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#### 4-(4-(Dimethylamino)phenyl)spiro[4.5]deca-3,6,9-triene-2,8-

dione (10e). Synthesised using general procedure C from ynone 9e (32 mg, 0.109 mmol) and SnCl<sub>2</sub>.2H<sub>2</sub>O (2.5 mg, 0.0109 mmol) for 20 h at RT. Purification by flash column chromatography (2:1 petrol:EtOAc) afforded the *title compound* 10e as a yellow solid (29 mg, 95%); mp. 199–201 °C; R<sub>f</sub> 0.20 (1:1 petrol:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 1656, 1636, 1581, 1548, 1500, 1353, 1182, 1156, 719;  $\delta_{\rm H}$  (400 MHz, CDCl<sub>3</sub>) 2.72 (2 H, s), 3.02 (6 H, s), 6.46 (2 H, d, *J* = 10.0), 6.55 (1 H, s), 6.58 (2 H, d, *J* = 9.0), 6.98 (2 H, d, *J* = 10.0), 7.43 (2 H, d, *J* = 9.0);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 39.9, 46.7, 50.9, 111.3, 119.9, 124.0, 129.2, 129.5, 152.3, 152.9, 173.3, 185.0, 203.0; HRMS (ESI<sup>+</sup>): Found: 280.1334; C<sub>18</sub>H<sub>18</sub>NO<sub>2</sub> (MH<sup>+</sup>) Requires 280.1332 (0.8 ppm error). Spectroscopic data matched those previously reported in the literature.<sup>10a</sup>

1-(4-Methoxyphenyl)-4-(thiophen-2-yl)but-3-yn-2-one (9f). Synthesised using general procedure B from 2ethynylthiophene<sup>17</sup> (303 mg, 2.80 mmol) and N-methoxy-2-(4methoxyphenyl)-N-methylacetamide<sup>18</sup> (391 mg, 1.87 mmol). Purification by flash column chromatography afforded the title compound 9f as a pale yellow oil (310 mg, 65%); Rf 0.73 (1:1 petrol:EtOAc);  $v_{max}$  (thin film)/cm<sup>-1</sup> 2148, 1636, 1586, 1489, 1230, 1019, 704;  $\delta_{H}$  (400 MHz, CDCl<sub>3</sub>) 3.80 (3 H, s), 3.85 (2 H, s), 6.90 (2 H, d, J = 8.5), 7.03 (1 H, dd, J = 5.0, 3.5) 7.22 (2 H, d, J = 8.5), 7.40 (1 H, d, J = 3.5), 7.47 (1 H, d, J = 5.0);  $\delta_c$  (100 MHz, CDCl<sub>3</sub>) 50.9, 55.2, 86.7, 92.4, 114.1, 119.6, 125.1, 127.6, 130.8, 131.8, 136.7, 158.9, 189.1; HRMS (ESI<sup>+</sup>): Found: 257.0625;  $C_{15}H_{13}O_{2}S$  (MH<sup>+</sup>) Requires 257.0631 (1.7 ppm error).

**4-(Thiophen-2-yl)spiro[4.5]deca-3,6,9-triene-2,8-dione** (10f). Synthesised using general procedure C from ynone **9f** (40 mg, 0.156 mmol) and copper(II) triflate (56.4 mg, 0.156 mmol) for 20 h at RT. Purification by flash column chromatography (2:1 petrol:EtOAc) afforded the *title compound* **10f** as a pale yellow oil (28 mg, 73%); R<sub>f</sub> 0.50 (1:1 petrol:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 1691, 1661, 1576, 1246, 1027, 907, 859, 724; δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>) 2.77 (2 H, s), 6.49 (2 H, d, J = 10.0), 6.58 (1 H, s), 6.92 (2 H, d, J = 10.0), 7.03 (1 H, dd, J = 4.5, 3.5) 7.32 (1 H, d, J = 3.5), 7.52 (1 H, d, J = 4.5); δ<sub>C</sub> (100 MHz, CDCl<sub>3</sub>) 46.3, 50.9, 127.3, 128.7, 130.2, 130.5, 131.4, 135.8, 150.9, 166.3, 184.7, 202.6; HRMS (ESI<sup>+</sup>): Found: 243.0480; C<sub>14</sub>H<sub>11</sub>O<sub>2</sub>S (MH<sup>+</sup>) Requires 243.0474 (-2.3 ppm error).

*N*-Methoxy-2-(4-methoxyphenyl)-*N*-methylbutanamide (S1). Synthesised using general procedure A from 2-(4-methoxyphenyl)butanoic acid<sup>19</sup> (1.07 g, 5.51 mmol) affording the *title compound* S1 as a colourless oil (1.31 g, 100%); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 1656, 1510, 1461, 1380, 1247, 1178, 997, 822;  $\delta_{\rm H}$  (400 MHz, CDCl<sub>3</sub>) 0.85 (3 H, t, *J* = 7.5), 1.64–1.75 (1 H, m),

 $\begin{array}{l} 1.98-2.10 \ (1 \ H, \ m), \ 3.14 \ (3 \ H, \ s), \ 3.49 \ (3 \ H, \ s), \ 3.76 \ (3 \ H, \ s), \\ 3.78-3.86 \ (1 \ H, \ m), \ 6.82 \ (2 \ H, \ d, \ J = 8.5), \ 7.23 \ (2 \ H, \ d, \ J = 8.5); \\ \delta_{C} \ (100 \ MHz, \ CDCl_{3}) \ 12.2, \ 27.2, \ 32.1, \ 48.3, \ 55.1, \ 61.2, \ 113.8, \\ 129.1, \ 132.2, \ 158.4, \ 175.0; \ HRMS \ (ESI^+): \ Found: \ 238.1438; \\ C_{13}H_{20}NO_{3} \ (MH^+) \ Requires \ 238.1438 \ (0 \ ppm \ error). \end{array}$ 

**1,4-Bis(4-methoxyphenyl)hex-1-yn-3-one** (9g). Synthesised using general procedure B from 4-ethynyl-anisole (0.41 mL, 3.17 mmol) and Weinreb amide **S1** (500 mg, 2.11 mmol). Purification by flash column chromatography afforded the *title compound* **9g** as a yellow oil (482 mg, 74%); R<sub>f</sub> 0.71 (1:1 petrol:EtOAc);  $v_{max}$  (thin film)/cm<sup>-1</sup> 2188, 1658, 1601, 1508, 1248, 1058, 1027, 831, 540;  $\delta_{H}$  (400 MHz, CDCl<sub>3</sub>) 0.91 (3 H, t, *J* = 7.5), 1.77–1.89 (1 H, m), 2.16–2.27 (1 H, m), 3.63–3.67 (1 H, m), 3.79 (3 H, s), 3.82 (3 H, s), 6.85 (2 H, d, *J* = 9.0), 6.89 (2 H, d, *J* = 9.0), 7.24 (2 H, d, *J* = 9.0), 7.41 (2 H, d, *J* = 9.0);  $\delta_{C}$  (100 MHz, CDCl<sub>3</sub>) 12.0, 24.8, 55.2, 55.4, 61.7, 87.5, 93.5, 111.9, 114.1, 114.2, 129.7, 130.0, 135.0, 158.9, 161.5, 188.4; HRMS (ESI<sup>+</sup>): Found: 309.1490; C<sub>20</sub>H<sub>21</sub>O<sub>3</sub> (MH<sup>+</sup>) Requires 309.1485 (-1.6 ppm error).

#### 1-Ethyl-4-(4-methoxyphenyl)spiro[4.5]deca-3,6,9-triene-2,8-

**dione (10g).** Synthesised using general procedure C from ynone **9g** (60.0 mg, 0.195 mmol) and copper(II) triflate (70.5 mg, 0.195 mmol) for 20 h at RT. Purification by flash column chromatography (2:1 petrol:EtOAc) afforded the *title compound* **10g** as a pale brown oil (43 mg, 75%); R<sub>f</sub> 0.50 (1:1 petrol:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 1696, 1661, 1590, 1509, 1257, 1177, 1030, 908, 832, 725;  $\delta_{\rm H}$  (400 MHz, CDCl<sub>3</sub>) 0.97 (3 H, t, *J* = 7.5), 1.25–1.35 (1 H, m), 1.75–1.84 (1 H, m), 2.66 (1 H, t, *J* = 7.0), 3.81 (3 H, s), 6.47 (1 H, dd, *J* = 10.0, 1.5), 6.56 (1 H, s), 6.56 (1 H, dd, *J* = 10.0, 3.0), 7.44 (2 H, d, *J* = 9.0);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 12.6, 20.0, 55.4, 55.8, 58.9, 114.3, 125.6, 126.9, 129.3, 130.0, 131.6, 151.0, 152.2, 162.1, 171.5, 185.3, 205.1; HRMS (ESI<sup>+</sup>): Found: 295.1324; C<sub>19</sub>H<sub>19</sub>O<sub>3</sub> (MH<sup>+</sup>) Requires 295.1329 (1.6 ppm error).

#### 2-(2,4-Dimethoxyphenyl)-N-methoxy-N-methylacetamide

(S2). Synthesised using general procedure A from 2-(2,4-dimethoxyphenyl)acetic acid (981 mg, 5.00 mmol) affording the *title compound* S2 as a pale yellow oil (1.13 g, 91%); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 1641, 1590, 1486, 1442, 1273, 1191, 1139, 1021;  $\delta_{H}$  (400 MHz, CDCl<sub>3</sub>) 3.19 (3 H, s), 3.67 (3 H, s), 3.69 (2 H, s), 3.78 (6 H, s), 6.42–6.47 (2 H, m), 7.07–7.11 (1 H, m);  $\delta_{c}$  (100 MHz, CDCl<sub>3</sub>) 32.4, 32.7, 55.3, 55.4, 61.1, 98.5, 104.1, 116.1, 131.1, 158.2, 159.8, 173.0; HRMS (ESI<sup>+</sup>): Found: 240.1232; C<sub>12</sub>H<sub>18</sub>NO<sub>4</sub> (MH<sup>+</sup>) Requires 240.1230 (1.0 ppm error).

#### 1-(2,4-Dimethoxyphenyl)-4-(4-methoxyphenyl)but-3-yn-2-

one (9h). Synthesised using general procedure B from 4ethynyl-anisole (741 mg, 5.61 mmol) and Weinreb amide S2 (894 mg, 3.74 mmol). Purification by trituration with ether afforded the *title compound* 9h as a pale yellow crystalline solid (789 mg, 68%); mp. 102–104 °C; R<sub>f</sub> 0.68 (1:1 petrol:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 2184, 1664, 1601, 1589, 1508, 1256, 1211, 1124, 1071, 1027, 835, 786, 575;  $\delta_{\rm H}$  (400

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 $\begin{array}{l} \mathsf{MHz},\mathsf{CDCI}_3)\ 3.77-3.84\ (11\ \mathsf{H},\ \mathsf{m}),\ 6.46-6.50\ (2\ \mathsf{H},\ \mathsf{m}),\ 6.84\ (2\ \mathsf{H},\\ \mathsf{d},\ J=8.5),\ 7.11\ (1\ \mathsf{H},\ \mathsf{d},\ J=8.5),\ 7.37\ (2\ \mathsf{H},\ \mathsf{d},\ J=8.5);\ \delta_{\mathsf{C}}\ (100\ \mathsf{MHz},\ \mathsf{CDCI}_3)\ 46.0,\ 55.3,\ 55.3,\ 55.4,\ 87.7,\ 92.7,\ 98.5,\ 104.2,\\ 111.9,\ 114.2,\ 115.1,\ 131.7,\ 135.1,\ 158.7,\ 160.4,\ 161.5,\ 186.2;\\ \mathsf{HRMS}\ (\mathsf{ESI}^+):\ \mathsf{Found:}\ 311.1284;\ C_{19}\mathsf{H}_{19}\mathsf{O}_4\ (\mathsf{MH}^+)\ \mathsf{Requires}\\ 311.1278\ (2.1\ \mathsf{ppm\ error}).\end{array}$ 

#### 6-Methoxy-4-(4-methoxyphenyl)spiro[4.5]deca-3,6,9-triene-

**2,8-dione (10h).** Synthesised using general procedure C from ynone **9h** (60.3 mg, 0.200 mmol) and SnCl<sub>2</sub>.2H<sub>2</sub>O (78 mg, 0.200 mmol) for 20 h at RT. Purification by flash column chromatography (2:1 petrol:EtOAc, then 1:1 petrol:EtOAc) afforded the *title compound* **10h** as a white solid (51 mg, 89%); mp. 169–171 °C; R<sub>f</sub> 0.19 (1:1 petrol:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 1689, 1652, 1588, 1360, 1244, 1177, 1027, 989, 858, 840;  $\delta_{\rm H}$  (400 MHz, CDCl<sub>3</sub>) 2.61 (1 H, d, *J* = 18.0), 2.86 (1 H, d, *J* = 18.0), 3.65 (3 H, s), 3.79 (3 H, s), 5.76 (1 H, d, *J* = 1.5), 6.34 (1 H, d, *J* = 10.0, 1.5), 6.61 (1 H, s), 6.64 (1 H, d, *J* = 10.0), 6.83 (2 H, d, *J* = 9.0), 7.43 (2 H, d, *J* = 9.0);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 47.7, 52.5, 55.4, 56.2, 103.4, 114.3, 125.1, 128.3, 128.4, 128.9, 147.4, 162.1, 171.6, 175.5, 187.2, 203.6; HRMS (ESI<sup>+</sup>): Found: 297.1112; C<sub>18</sub>H<sub>17</sub>O<sub>4</sub> (MH<sup>+</sup>) Requires 297.1121 (1.9 ppm error).

#### 4-(2,4-Dimethoxyphenyl)-1-(4-methoxyphenyl)but-3-yn-2-

**one (9i).** Synthesised using general procedure B from 1ethynyl-2,4-dimethoxybenzene<sup>20</sup> (420 mg, 2.59 mmol) and *N*methoxy-2-(4-methoxyphenyl)-*N*-methylacetamide<sup>21</sup> (361 mg, 1.73 mmol). Purification by flash column chromatography afforded the *title compound* **9i** as a pale yellow oil (340 mg, 63%); R<sub>f</sub> 0.60 (1:1 petrol:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 2185, 1652, 1600, 1505, 1296, 1244, 1210, 1026, 819;  $\delta_{\rm H}$  (400 MHz, CDCl<sub>3</sub>) 3.79 (3 H, s), 3.82 (3 H, s), 3.84–3.87 (5 H, m), 6.39 (1 H, d, *J* = 2.0), 6.45 (1 H, dd, *J* = 8.5, 2.0), 6.86 (2 H, d, *J* = 8.5), 7.25 (2 H, d, *J* = 8.5), 7.34 (1 H, d, *J* = 8.5);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 51.3, 55.2, 55.5, 55.7, 91.3, 91.9, 98.2, 101.5, 105.4, 114.0, 125.6, 130.9, 136.5, 158.7, 163.2, 163.6, 185.5; HRMS (ESI<sup>+</sup>): Found: 311.1272; C<sub>19</sub>H<sub>19</sub>O<sub>4</sub> (MH<sup>+</sup>) Requires 311.1278 (1.9 ppm error).

#### 4-(2,4-Dimethoxyphenyl)spiro[4.5]deca-3,6,9-triene-2,8-

**dione (10i).** Synthesised using general procedure C from ynone **9i** (55.0 mg, 0.177 mmol) and SnCl<sub>2</sub>.2H<sub>2</sub>O (40.0 mg, 0.177 mmol) for 20 h at RT. Purification by flash column chromatography (2:1 petrol:EtOAc, then 1:1 petrol:EtOAc) afforded the *title compound* **10i** as a pale brown solid (48 mg, 91%); mp. 172–174 °C R<sub>f</sub> 0.19 (1:1 petrol:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 1688, 1660, 1605, 1551, 1233, 1213, 1026, 859;  $\delta_{\rm H}$ (400 MHz, CDCl<sub>3</sub>) 2.67 (2 H, s), 3.80 (3 H, s), 3.84 (3 H, s), 6.37 (1 H, dd, *J* = 8.5, 2.5), 6.40 (2 H, d, *J* = 10.0), 6.46 (1 H, d, *J* = 2.5), 6.95 (2 H, d, *J* = 10.0), 6.97 (1 H, s), 7.26 (1 H, d, *J* = 8.5);  $\delta_{\rm C}$ (100 MHz, CDCl<sub>3</sub>) 46.1, 52.4, 55.4, 55.5, 98.9, 104.4, 115.0, 129.2, 130.2, 131.6, 152.9, 160.1, 163.2, 168.8, 184.9, 204.7; HRMS (ESI<sup>+</sup>): Found: 297.1113; C<sub>18</sub>H<sub>17</sub>O<sub>4</sub> (MH<sup>+</sup>) Requires 297.1121 (2.6 ppm error).

**1-(4-Methoxyphenyl)-4-(phenylthio)but-3-yn-2-one** (9j). Synthesised using general procedure B from ethynyl(phenyl)sulfane<sup>22</sup> (671 mg, 5.00 mmol) and *N*-methoxy2-(4-methoxyphenyl)-*N*-methylacetamide<sup>21</sup> (697 mg, 3.33 mmol). Purification by flash column chromatography afforded the *title compound* **9j** as a yellow oil (313 mg, 33%); R<sub>f</sub> 0.81 (1:1 petrol:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 2115, 1651, 1510, 1246, 1176, 1120, 738, 686;  $\delta_{\rm H}$  (400 MHz, CDCl<sub>3</sub>) 3.79 (2 H, s), 3.80 (3 H, s), 6.89 (2 H, d, J = 8.5), 7.17–7.35 (7 H, m);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 50.2, 55.2, 87.6, 100.7, 114.2, 125.0, 127.0, 127.8, 129.5, 129.6, 130.9, 158.9, 183.3; HRMS (ESI<sup>+</sup>): Found: 283.0786; C<sub>17</sub>H<sub>15</sub>O<sub>2</sub>S (MH<sup>+</sup>) Requires 283.0787 (0.1 ppm error).

**4-(Phenylthio)spiro[4.5]deca-3,6,9-triene-2,8-dione** (10j). Synthesised using general procedure C from ynone **9j** (70.6 mg, 0.250 mmol) and copper(II) triflate (90.4 mg, 0.250 mmol) for 2 h at RT. Purification by flash column chromatography (2:1 petrol:EtOAc, then 1:1 petrol:EtOAc) afforded the *title compound* **10j** as a pale orange solid (43 mg, 64%); mp. 113–115 °C; R<sub>f</sub> 0.25 (1:1 petrol:ethyl acetate); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 1687, 1665, 1548, 860, 752; δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>) 2.74 (2 H, s), 5.63 (1 H, s), 6.47 (2 H, d, *J* = 10.0), 6.79 (2 H, d, *J* = 10.0), 7.42–7.49 (5 H, m); δ<sub>C</sub> (100 MHz, CDCl<sub>3</sub>) 46.2, 51.3, 125.8, 128.4, 130.2, 130.4, 130.6, 134.5, 149.2, 182.5, 184.5, 199.8; HRMS (ESI<sup>+</sup>): Found: 269.0621; C<sub>16</sub>H<sub>13</sub>O<sub>2</sub>S (MH<sup>+</sup>) Requires 269.0631 (3.0 ppm error).

1,5-Bis(4-methoxyphenyl)pent-1-yn-3-one (9k). Synthesised using general procedure B from 4-ethynylanisole (488 mg, 3.70 N-methoxy-3-(4-methoxyphenyl)-Nmmol) and methylpropanamide<sup>23</sup> (550 mg, 2.46 mmol). Purification by flash column chromatography afforded the title compound 9k as a yellow solid (500 mg, 69%); mp. 58-60 °C; R<sub>f</sub> 0.80 (1:1 petrol:EtOAc);  $v_{max}$  (thin film)/cm<sup>-1</sup> 2185, 1659, 1601, 1508, 1293, 1245, 117,1084, 1026, 830;  $\delta_{\rm H}$  (400 MHz,  ${\rm CDCl}_{\rm 3}$ ) 2.92– 3.02 (4 H, m), 3.78 (3 H, s), 3.83 (3 H, s), 6.83 (2 H, d, J = 8.5), 6.89 (2 H, d, J = 8.5), 7.14 (2 H, d, J = 8.5), 7.51 (2 H, d, J = 8.5);  $\delta_{c}$  (100 MHz, CDCl<sub>3</sub>) 29.2, 47.1, 55.2, 55.4, 87.7, 92.3, 111.6, 113.9, 114.3, 129.3, 132.4, 135.1, 158.0, 161.6, 187.1; HRMS (ESI<sup>+</sup>): Found: 295.1317; C<sub>19</sub>H<sub>19</sub>O<sub>3</sub> (MH<sup>+</sup>) Requires 295.1329 (3.7 ppm error).

#### 7-(4-Methoxyphenyl)spiro[5.5]undeca-1,4,7-triene-3,9-dione

**(10k).** Synthesised using general procedure C from ynone **9k** (62.0 mg, 0.204 mmol) and copper(II) triflate (73.7 mg, 0.204 mmol) for 20 h at 50 °C. Purification by flash column chromatography (1:1 petrol:EtOAc) afforded the *title compound* **10k** as a pale yellow solid (46 mg, 78%); mp. 165–167 °C; R<sub>f</sub> 0.25 (1:1 petrol:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 1657, 1623, 1603, 1510, 1243, 1178, 1030, 859, 731;  $\delta_{\rm H}$  (400 MHz, CDCl<sub>3</sub>) 2.25 (2 H, t, *J* = 6.5), 2.68 (2 H, t, *J* = 6.5), 3.78 (3 H, s), 6.30 (1 H, s), 6.42 (2 H, d, *J* = 10.0), 6.79 (2 H, d, *J* = 9.0), 7.06 (2 H, d, *J* = 10.0), 7.19 (2 H, d, *J* = 9.0);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 34.0, 37.7, 45.5, 55.3, 114.0, 127.7, 128.1, 130.1, 130.4, 152.6, 159.2, 161.0, 184.7, 196.9; HRMS (ESI<sup>\*</sup>): Found: 281.1179; C<sub>18</sub>H<sub>17</sub>O<sub>3</sub> (MH<sup>+</sup>) Requires 281.1172 (2.5 ppm error).

#### 1-(4'-Methoxybiphenyl-2-yl)-3-(4-methoxyphenyl)prop-2-yn-

**1-one (9I).** Synthesised using general procedure B from 4-ethynylanisole (190 mg, 1.44 mmol) and *N*,4'-dimethoxy-*N*-

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Published on 23 November 2016. Downloaded by Athabasca University on 23/11/2016 12:57:49

methyl-[1,1'-biphenyl]-2-carboxamide<sup>24</sup> (260 mg, 0.958). Purification by flash column chromatography (10:1 petrol:EtOAc, then 5:1 petrol:EtOAc) afforded the title compound 9I as a pale yellow oil (141 mg, 43%); Rf 0.70 (1:1 petrol:EtOAc);  $v_{max}$  (thin film)/cm<sup>-1</sup> 2184, 1620, 1599, 1508, 1289, 1248, 1027, 999, 830, 760;  $\delta_{\rm H}$  (400 MHz,  ${\rm CDCl}_3$ ) 3.77 (3 H, s), 3.80 (3 H, s), 6.79 (2 H, d, J = 9.0), 6.94 (2 H, d, J = 8.5), 7.22 (2 H, d, J = 9.0), 7.35 (2 H, d, J = 8.5), 7.40-7.45 (2 H, m), 7.53–7.58 (1 H, m), 7.92 (1 H, d, J = 7.5);  $\delta_c$  (100 MHz, CDCl<sub>3</sub>) 55.3, 55.4, 88.9, 94.9, 112.0, 113.8, 114.0, 127.0, 129.9, 130.7, 130.9, 131.9, 132.9, 135.0, 138.1, 142.3, 159.4, 161.4, 180.8; HRMS (ESI<sup>+</sup>): Found: 343.1324; C<sub>23</sub>H<sub>19</sub>O<sub>3</sub> (MH<sup>+</sup>) Requires 343.1329 (1.0 ppm error).

#### 2'-(4-Methoxyphenyl)-4'H-spiro[cyclohexa[2,5]diene-1,1'-

**naphthalene]-4,4'-dione (10l).** Synthesised using general procedure C from ynone **9l** (66.0 mg, 0.193 mmol) and copper(II) triflate (69.6 mg, 0.193 mmol) for 48 h at RT. Purification by flash column chromatography (2:1 petrol:EtOAc) afforded the *title compound* **10l** as a pale yellow oil (47 mg, 74%); R<sub>f</sub> 0.25 (1:1 petrol:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 1655, 1602, 1510, 1331, 1251, 1031, 836; δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>) 3.797 (3 H, s), 6.44 (2 H, d, *J* = 9.5), 6.72 (1 H, s), 6.74 (2 H, d, *J* = 9.5), 6.82 (2 H, d, *J* = 9.0), 7.25–7.29 (3 H, m), 7.48–7.57 (2 H, m), 8.25 (1 H, d, *J* = 7.0); δ<sub>C</sub> (100 MHz, CDCl<sub>3</sub>) 50.7, 55.3, 113.7, 127.3, 128.2, 128.7, 128.9, 129.6, 130.0, 130.0, 130.2, 133.2, 138.3, 150.0, 156.0, 160.6, 183.6, 185.2; HRMS (ESI<sup>\*</sup>): Found: 329.1170; C<sub>22</sub>H<sub>17</sub>O<sub>3</sub> (MH<sup>\*</sup>) Requires 329.1172 (0.8 ppm error).

**2-(4-)-***N***-methoxy-***N***-methylacetamide (S3).** Synthesised using general procedure A2 from 2-(4-hydroxyphenyl)acetic acid (2.40 g, 15.8 mmol) stirring at RT for 1 h. Afforded the *title compound* S3 as a white solid (3.00 g, 100%); mp 110–112 °C; R<sub>f</sub> 0.58 (9:1 EtOAc:hexane); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 3264, 1631, 1614, 1594, 1515, 1446, 1233, 1172, 1002, 798;  $\delta_{\rm H}$  (400 MHz, CDCl<sub>3</sub>) 3.22 (3 H, s), 3.65 (3 H, s), 3.70 (2 H, s), 6.68 (2 H, d, *J* = 8.5), 7.07 (2 H, d, *J* = 8.5);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 32.3, 38.2, 61.3, 115.6, 125.9, 130.4, 155.2, 173.3; HRMS (ESI<sup>+</sup>): Found: 218.0788; C<sub>10</sub>H<sub>13</sub>NNaO<sub>3</sub> (MNa<sup>+</sup>) Requires 218.0788 (-0.3 ppm error), Found: 196.0975; C<sub>10</sub>H<sub>14</sub>NO<sub>3</sub> (MH<sup>+</sup>) Requires 196.0968 (-3.2 ppm error).

#### 1-(4-Hydroxyphenyl)-4-phenylbut-3-yn-2-one

(11c).

Synthesised using general procedure B2 from phenylacetylene (0.34 mL, 3.07 mmol) and Weinreb amide **S3** (200 mg, 1.02 mmol) stirring at RT for 30 min. Purification by flash column chromatography (9:1 hexane:EtOAc, then 1:1 hexane:EtOAc) afforded the *title compound* **11c** as a pale yellow solid (135 mg, 56%); mp 96–98 °C; R<sub>f</sub> 0.51 (6:4 hexane:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 3368, 2202, 1655, 1514, 1224, 1079, 758, 688;  $\delta_{\rm H}$  (400 MHz, CDCl<sub>3</sub>) 3.87 (2 H, s), 5.42 (1 H, br s), 6.83–6.88 (2 H, m), 7.16–7.21 (2 H, m), 7.33–7.39 (2 H, m), 7.42–7.50 (3 H, m);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 51.3, 87.7, 93.3, 115.7, 119.7, 125.1, 128.6, 130.9, 131.1, 133.1, 155.1, 186.1; HRMS (ESI<sup>+</sup>): Found: 259.0731; C<sub>16</sub>H<sub>12</sub>NaO<sub>2</sub> (MNa<sup>+</sup>) Requires 259.0730 (-0.6 ppm

error), Found: 237.0919;  $C_{16}H_{13}O_2$  (MH<sup>+</sup>) Requires 237.0910 (-3.8 ppm error).

# 4-Phenylspiro[4.5]deca-3,6,9-triene-2,8-dione (10c).

Synthesised using general procedure C2 from ynone **11c** (100 mg, 0.423 mmol) and AgNO<sub>3</sub>·SiO<sub>2</sub> (719 mg, 0.0423 mmol) for 24 h at 40 °C. Afforded the *title compound* **10c** without further purification as a pale brown solid (94.0 mg, 94%); mp 124–126 °C; R<sub>f</sub> 0.31 (1:1 hexane:EtOAc);  $v_{max}$  (thin film)/cm<sup>-1</sup> 3068, 1693, 1658, 1592, 1251, 859, 764;  $\delta_{H}$  (400 MHz, CDCl<sub>3</sub>) 2.80 (2 H, s), 6.49 (2 H, d, *J* = 10.0), 6.71 (1 H, s), 6.96 (2 H, d, *J* = 10.0), 7.34–7.40 (2 H, m), 7.42–7.48 (1 H, m), 7.49–7.54 (2 H, m);  $\delta_{C}$  (100 MHz, CDCl<sub>3</sub>) 46.9, 51.2, 127.4, 129.0, 129.9, 130.0, 131.6, 132.9, 151.4, 173.9, 184.7, 203.3; HRMS (ESI<sup>+</sup>): Found: 259.0732; C<sub>16</sub>H<sub>12</sub>NaO<sub>2</sub> (MNa<sup>+</sup>) Requires 259.0730 (–0.9 ppm error). Spectroscopic data matched those previously reported in the literature.<sup>25</sup>

#### 1-(4-Hydroxyphenyl)-4-(4-methoxyphenyl)but-3-yn-2-one

(11d). Synthesised using general procedure B from 1-ethynyl-4-methoxybenzene (983 mg, 7.44 mmol) and Weinreb amide S3 (484 mg, 2.48 mmol) stirring at RT for 1 h. Purification by flash column chromatography (9:1 hexane:EtOAc, then 7:3 hexane:EtOAc) afforded the *title compound* 11d as a yellow solid (502 mg, 76%); mp 86–88 °C; R<sub>f</sub> 0.62 (1:1 hexane:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 3353, 2195, 1651, 1600, 1510, 1254, 1170, 1076, 834;  $\delta_{\rm H}$  (400 MHz, CDCl<sub>3</sub>) 3.83 (3 H, s), 3.85 (2 H, s), 5.52 (1 H, br s), 6.86 (4 H, m), 7.17 (2 H, d, *J* = 8.0), 7.41 (2 H, d, *J* = 8.5);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 51.1, 55.4, 87.8, 94.7, 111.5, 114.3, 115.6, 125.4, 131.1, 135.2, 155.1, 161.7, 186.3; HRMS (ESI<sup>+</sup>): Found: 289.0839; C<sub>17</sub>H<sub>14</sub>NaO<sub>3</sub> (MNa<sup>+</sup>) Requires 289.0835 (-1.4 ppm error).

#### 4-(4-Methoxyphenyl)spiro[4.5]deca-3,6,9-triene-2,8-dione

(10d). Synthesised using general procedure C2 from ynone 11d (100 mg, 0.376 mmol) and  $AgNO_3 \cdot SiO_2$  (638 mg, 0.0376 mmol) for 3 h at 40 °C. Afforded the *title compound* 10d without further purification as a brown solid (100 mg, 100%). Data for this compound is reported above.

#### 2-(4-Hydroxy-3-methoxyphenyl)-N-methoxy-N-

**methylacetamide (S4).** Synthesised using general procedure A2 from 2-(4-hydroxy-3-methoxyphenyl)acetic acid (1.15 g, 6.34 mmol) stirring at RT for 1 h. Afforded the *title compound* **S4** as a clear and colourless oil (810 mg, 48%); R<sub>f</sub> 0.21 (1:1 hexane:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 3316, 2939, 1639, 1514, 1432, 1271, 1200, 1151, 1033;  $\delta_{\rm H}$  (400 MHz, CDCl<sub>3</sub>) 3.19 (3 H, s), 3.62 (3 H, s), 3.70 (2 H, s), 3.87 (3 H, s), 5.35 (1 H, br s), 6.75 (1 H, d, *J* = 8.0), 6.82–6.86 (2 H, m);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 32.2, 38.8, 55.8, 61.3, 111.7, 114.2, 122.1, 126.5, 144.5, 146.5, 172.7; HRMS (ESI<sup>+</sup>): Found: 248.0884; C<sub>111</sub>H<sub>15</sub>NNaO<sub>4</sub> (MNa<sup>+</sup>) Requires 248.0893 (3.7 ppm error), Found: 226.1070; C<sub>11</sub>H<sub>16</sub>NO<sub>4</sub> (MH<sup>+</sup>) Requires 226.1074 (1.6 ppm error).

#### 1-(4-Hydroxy-3-methoxyphenyl)-4-(4-methoxyphenyl)but-3-

**yn-2-one (11m).** Synthesised using general procedure B2 from 1-ethynyl-4-methoxybenzene (880 mg, 6.66 mmol) and

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DOI: 10.1039/C6OB02426B

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Weinreb amide **S4** (500 mg, 2.22 mmol) stirring at RT for 1 h. Purification by flash column chromatography (9:1 hexane:EtOAc, then 7:3 hexane:EtOAc) afforded the *title compound* **11m** as a yellow solid (443 mg, 58%); mp 61–63 °C; R<sub>f</sub> 0.20 (7:3 hexane:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 3437, 2195, 1655, 1601, 1509, 1254, 1237, 1170;  $\delta_{\rm H}$  (400 MHz, CDCl<sub>3</sub>) 3.84 (5 H, s), 3.89 (3 H, s), 5.63 (1 H, br s), 6.78–6.95 (5 H, m), 7.43 (2 H, d, *J* = 8.5);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 51.7, 55.4, 55.9, 87.7, 94.1, 111.6, 112.0, 114.3, 114.5, 122.8, 125.2, 135.1, 144.9, 146.6, 161.7, 185.7; HRMS (ESI<sup>+</sup>): Found: 319.0939; C<sub>18</sub>H<sub>16</sub>NaO<sub>4</sub> (MNa<sup>+</sup>) Requires 319.0941 (0.7 ppm error).

#### 7-Methoxy-4-(4-methoxyphenyl)spiro[4.5]deca-3,6,9-triene-

**2,8-dione (10m).** Synthesised using general procedure C2 from ynone **11m** (59.0 mg, 0.199 mmol) and AgNO<sub>3</sub>·SiO<sub>2</sub> (338 mg, 0.0199 mmol) for 24 h at 40 °C. Purification by flash column chromatography (8:2 hexane:EtOAc) afforded the *title compound* **10m** an off-white oil (50.9 mg, 86%); R<sub>f</sub> 0.14 (1:1 hexane:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 1691, 1664, 1636, 1603, 1587, 1509, 1258, 1208, 1177, 831;  $\delta_{\rm H}$  (400 MHz, CDCl<sub>3</sub>) 2.78 (1 H, d, *J* = 18.5), 2.86 (1 H, d, *J* = 18.5), 3.66 (3 H, s), 3.83 (3 H, s), 5.86 (1 H, d, *J* = 2.5), 6.50 (1 H, d, *J* = 9.5), 6.61 (1 H, s), 6.85 (2 H, d, *J* = 8.5), 6.97 (1 H, dd, *J* = 9.5, 2.5), 7.48 (2 H, d, *J* = 8.5);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 48.0, 51.6, 55.2, 55.4, 114.3, 119.4, 125.3, 127.1, 129.0, 129.4, 151.7, 152.4, 162.2, 173.7, 180.1, 203.4; HRMS (ESI<sup>+</sup>): Found: 319.0947; C<sub>18</sub>H<sub>16</sub>NaO<sub>4</sub> (MNa<sup>+</sup>) Requires 319.0941 (-2.0 ppm error).

**1-(4-Hydroxyphenyl)oct-3-yn-2-one(11n).** Synthesised using general procedure B2 from hex-1-yne (0.35 mL, 3.07 mmol) and Weinreb amide **S3** (200 mg, 1.02 mmol) stirring at RT for 1 h. Purification by flash column chromatography (9:1 hexane:EtOAc, then 7:3 hexane:EtOAc) afforded the *title compound* **11n** as a yellow oil (181 mg, 82%); R<sub>f</sub> 0.76 (1:1 hexane:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 3373, 2959, 2933, 2209, 1652, 1514, 1224, 796;  $\delta_{\rm H}$  (400 MHz, CDCl<sub>3</sub>) 0.89 (3 H, t, *J* = 7.5), 1.35 (2 H, qt, *J* = 7.5, 7.5), 1.48 (2 H, tt, *J* = 7.5, 7.0), 2.32 (2 H, t, *J* = 7.0), 3.74 (2 H, s), 5.93 (1 H, br s), 6.80 (2 H, d, *J* = 8.0), 7.09 (2 H, d, *J* = 8.0);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 13.4, 18.6, 21.8, 29.5, 51.3, 80.7, 97.3, 115.6, 124.9, 130.9, 155.1, 186.7; HRMS (ESI<sup>+</sup>): Found: 239.1050; C<sub>14</sub>H<sub>16</sub>NaO<sub>2</sub> (MNa<sup>+</sup>) Requires 239.1043 (-3.2 ppm error).

#### 4-Butylspiro[4.5]deca-3,6,9-triene-2,8-dione(10n).

Synthesised using general procedure C2 from ynone **11n** (85.4 mg, 0.395 mmol) and AgNO<sub>3</sub>·SiO<sub>2</sub> (671 mg, 0.0395 mmol) for 24 h at RT. Afforded the *title compound* **10n** without further purification as a pale yellow solid (80.3 mg, 94%); mp 100–102 °C; R<sub>f</sub> 0.35 (1:1 hexane:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 2959, 2929, 2875, 2857, 1720, 1696, 1657, 1614, 1599, 1255, 1232, 862;  $\delta_{\rm H}$  (400 MHz, CDCl<sub>3</sub>) 0.90 (3 H, t, *J* = 7.5), 1.33 (2 H, qt, *J* = 7.5), 1.52 (2 H, tt, *J* = 7.5, 7.5), 2.10 (2 H, t, *J* = 7.5), 2.65 (2 H, s), 6.22 (1 H, s), 6.45 (2 H, d, *J* = 9.0), 6.66 (2 H, d, *J* = 9.0);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 13.7, 22.2, 28.8, 29.5, 45.0, 52.6, 130.58, 130.61, 150.0, 181.6, 184.9, 204.6; HRMS (ESI<sup>+</sup>): Found: 239.1043; C<sub>14</sub>H<sub>16</sub>NaO<sub>2</sub> (MNa<sup>+</sup>) Requires 239.1043 (-0.3 ppm error), Found: 217.1219; C<sub>14</sub>H<sub>17</sub>O<sub>2</sub> (MH<sup>+</sup>) Requires 217.1223

(2.0 ppm error). Spectroscopic data matched those previously reported in the literature.  $^{\rm 26}$ 

tert-Butyl (6-(4-hydroxyphenyl)-5-oxohex-3-yn-1yl)(methyl)carbamate (110). Synthesised using general procedure B2 from *tert*-butyl but-3-vn-1yl(methyl)carbamate<sup>10d</sup> (568 mg, 3.10 mmol) and Weinreb amide S3 (202 mg, 1.03 mmol) stirring at RT for 2.5 h. Purification by flash column chromatography (9:1 hexane:EtOAc, then 1:1 hexane:EtOAc) afforded the title compound 11o as a yellow oil (241 mg, 74%); R<sub>f</sub> 0.62 (1:1 hexane:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 3331, 2977, 2212, 1663, 1515, 1395, 1366, 1225, 1145, 730;  $\delta_{H}$  (400 MHz, CDCl<sub>3</sub>) 1.47 (9 H, s), 2.54 (2 H, t, J = 7.0), 2.86 (3 H, s), 3.36 (2 H, t, J = 7.0), 3.71 (2 H, s), 6.07 (1 H, br s), 6.81 (2 H, d, J = 8.0), 7.08 (2 H, d, J = 8.0); δ<sub>c</sub> (100 MHz, CDCl<sub>3</sub>) 18.6, 28.4, 35.0, 47.2, 51.2, 80.3, 81.7, 92.9, 115.8, 124.8, 130.9, 155.6, 155.6, 185.4; HRMS (ESI<sup>+</sup>): Found: 340.1522;  $C_{18}H_{23}NNaO_4$  (MNa<sup>+</sup>) Requires 340.1519 (-0.9 ppm error). Note: majority of peaks broadened in <sup>1</sup>H NMR spectrum due to presence of rotamers.

tert-Butvl (2-(3,8-dioxospiro[4.5]deca-1,6,9-trien-1yl)ethyl)(methyl)carbamate (10o). Synthesised using general procedure C2 from ynone 11o (73.5 mg, 0.232 mmol) and AgNO<sub>3</sub>·SiO<sub>2</sub> (394 mg, 0.0232 mmol) for 10 h at RT. Afforded the title compound 10o without further purification as a pale yellow oil (68.5 mg, 93%); R<sub>f</sub> 0.22 (1:1 hexane:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 2975, 1720, 1688, 1662, 1624, 1615, 1392, 1365, 1165, 1144, 860;  $\delta_H$  (400 MHz, CDCl<sub>3</sub>) 1.43 (9 H, s), 2.31 (2 H, t, J = 7.0), 2.62 (2 H, s), 2.81 (3 H, s), 3.39 (2 H, t, J = 7.0), 6.20 (1 H, s), 6.43 (2 H, d, J = 9.5), 6.65–6.73 (2 H, br m);  $\delta_c$ (100 MHz, CDCl<sub>3</sub>) 27.2, 28.4, 34.2, 45.1, 47.1, 52.8, 80.0, 130.9, 132.0, 149.4, 155.5, 176.9, 184.5, 203.8; HRMS (ESI<sup>+</sup>): Found: 340.1522; C<sub>18</sub>H<sub>23</sub>NNaO<sub>4</sub> (MNa<sup>+</sup>) Requires 340.1519 (-0.8 ppm error). Note: majority of peaks broadened in <sup>1</sup>H NMR spectrum due to presence of rotamers.

6-((tert-Butyldimethylsilyl)oxy)-1-(4-hydroxyphenyl)hex-3-yn-2-one (11p). To an oven-dried 100 mL round-bottom flask containing (but-3-yn-1-yloxy)(tert-butyl)dimethylsilane<sup>27</sup> (753 mg, 4.09 mmol) and freshly distilled THF (15 mL) at -78 °C under argon was added n-BuLi (1.3 mL, 4.3mmol, 2.5 M in hexanes) drop-wise over 10 min. After stirring at -78 °C for 60 min, the alkyne solution was transferred via cannula into an oven-dried round-bottom flask containing Weinreb amide S3 (266 mg, 1.36 mmol) in THF (15 mL) and stirred at -78 °C for 10 min. The resulting suspension was warmed to RT, quenched with saturated aqueous NH<sub>4</sub>Cl (20 mL), extracted successively with EtOAc (3 x 15 mL), and the combined organics washed with brine (20 mL), dried (MgSO<sub>4</sub>), and concentrated under vacuum to yield a crude product. The crude product was purified by flash column chromatography (9:1 hexane:EtOAc, then 6:4 hexane:EtOAc) to afford the title compound 11p as a yellow oil (367 mg, 84%);  $R_f 0.56$  (1:1 hexane:EtOAc);  $v_{max}$  (thin film)/cm<sup>-</sup> 3379, 2953, 2929, 2857, 2213, 1670, 1514, 1253, 1106, 836, 795, 778; δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>) 0.06 (6 H, s), 0.88 (9 H, s), 2.53 (2 H, t, J = 7.0), 3.71 (2 H, t, J = 7.0), 3.73 (2 H, s),

DOI: 10.1039/C6OB02426B Journal Name

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Published on 23 November 2016. Downloaded by Athabasca University on 23/11/2016 12:57:49

6.77 (2 H, app. d, J = 8.5), 7.06 (2 H, app. d, J = 8.5);  $\delta_{C}$  (100 MHz, CDCl<sub>3</sub>) -5.2, 18.4, 23.5, 25.9 , 51.3, 60.8, 81.5, 93.7, 115.7, 124.8, 131.0, 155.2, 186.3; HRMS (ESI<sup>+</sup>): Found: 341.1536;  $C_{18}H_{26}NaO_{3}Si$  (MNa<sup>+</sup>) Requires 341.1543 (2.3 ppm error).

#### 4-(2-((tert-Butyldimethylsilyl)oxy)ethyl)spiro[4.5]deca-3,6,9-

**triene-2,8-dione (10p).** Synthesised using general procedure C2 from ynone **11p** (55.0 mg, 0.170 mmol) and AgNO<sub>3</sub>·SiO<sub>2</sub> (293 mg, 0.0170 mmol) 16 h at RT. Purification by flash column chromatography (8:2 hexane:EtOAc, then 1:1 hexane:EtOAc) afforded the *title compound* **10p** as an orange solid (49.0 mg, 89%); R<sub>f</sub> 0.42 (1:1 hexane:EtOAc); mp 76–80 °C ; v<sub>max</sub> (thin film)/cm<sup>-1</sup> 2928, 2857, 1721, 1698, 1657, 1621, 1254, 1102, 864, 834, 775; δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>) 0.01 (6 H, s), 0.85 (9 H, s), 2.28 (2 H, dt, *J* = 6.0, 1.5), 2.26 (2 H, s), 3.75 (2 H, t, *J* = 6.0), 6.31 (1 H, t, *J* = 1.5), 6.42 (2 H, app. d, *J* = 10.0), 6.64 (2 H, app. d, *J* = 10.0); δ<sub>C</sub> (100 MHz, CDCl<sub>3</sub>) -5.35, 18.3, 25.9, 32.3, 44.9, 52.7, 60.6, 130.8, 132.0, 149.8, 178.0, 184.9, 204.8; HRMS (ESI<sup>+</sup>): Found: 341.1541; C<sub>18</sub>H<sub>26</sub>NaO<sub>3</sub>Si (MNa<sup>+</sup>) Requires 341.1543 (0.7 ppm error).

4-Cyclopropyl-1-(4-hydroxyphenyl)but-3-yn-2-one (11q). procedure Synthesised using general B2 from ethynylcyclopropane (0.40 mL, 4.61 mmol) and Weinreb amide S3 (300 mg, 1.54 mmol) stirring at RT for 1 h. Purification by flash column chromatography (1:1 hexane:EtOAc) afforded the title compound 11q as a white solid (276 mg, 90%); mp 81-83 °C; R<sub>f</sub> 0.59 (1:1 hexane:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 3367, 2201, 1647, 1514, 1222;  $\delta_{H}$  (400 MHz, CDCl<sub>3</sub>) 0.80–0.85 (2 H, m), 0.92-0.98 (2 H, m), 1.31-1.39 (1 H, m), 3.71 (2 H, ), 5.30 (1 H, br s), 6.80 (2 H, d, J = 8.0), 7.09 (2 H, d, J = 8.0);  $\delta_c$  (100 MHz, CDCl<sub>3</sub>) -0.3, 9.9, 51.1, 76.5, 101.6, 115.5, 125.3, 130.9, 154.9, 186.0; HRMS (ESI<sup>+</sup>): Found: 223.0734; C<sub>13</sub>H<sub>12</sub>NaO<sub>2</sub> (MNa<sup>+</sup>) Requires 223.0730 (-2.1 ppm error), Found: 201.0906;  $C_{13}H_{13}O_2$  (MH<sup>+</sup>) Requires 201.0910 (1.9 ppm error).

**4-Cyclopropylspiro[4.5]deca-3,6,9-triene-2,8-dione** (10q). Synthesised using general procedure C2 from ynone **11q** (101 mg, 0.504 mmol) and AgNO<sub>3</sub>·SiO<sub>2</sub> (857 mg, 0.0504 mmol) for 2 h at RT. Afforded the *title compound* **10q** without further purification as a white solid (100 mg, 99%); mp 109–111 °C; R<sub>f</sub> 0.45 (1:1 hexane:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 1689, 1666, 1624, 1605, 1401, 1252, 860;  $\delta_{\rm H}$  (400 MHz, CDCl<sub>3</sub>) 0.77–0.82 (2 H, m), 1.11–1.17 (2 H, m), 1.18–1.24 (1 H, m), 2.64 (2 H, s), 5.75 (1 H, s), 6.45 (2 H, d, *J* = 10.0), 6.72 (2 H, d, *J* = 10.0);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 11.0, 13.8, 45.0, 52.8, 123.5, 130.6, 150.0, 184.9, 185.6, 204.2; HRMS (ESI<sup>+</sup>): Found: 223.0733; C<sub>13</sub>H<sub>12</sub>NaO<sub>2</sub> (MNa<sup>+</sup>) Requires 223.0730 (–1.7 ppm error), Found: 201.0906; C<sub>13</sub>H<sub>13</sub>O<sub>2</sub> (MH<sup>+</sup>) Requires 201.0910 (2.2 ppm error.

4-Cyclopentyl-1-(4-hydroxyphenyl)but-3-yn-2-one (11r).
Synthesised using general procedure B2 from ethynylcyclopentane (0.36 mL, 3.07 mmol) and Weinreb amide
S3 (200 mg, 1.02 mmol) stirring at RT for 1 h. Purification by flash column chromatography (9:1 hexane:EtOAc, then 7:3 hexane:EtOAc) afforded the *title compound* 11r as a pale

yellow oil (207 mg, 89%); R<sub>f</sub> 0.74 (1:1 hexane:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 3376, 2961, 2871, 2205, 1650, 1514, 1224, 1172;  $\delta_{\rm H}$  (400 MHz, CDCl<sub>3</sub>) 1.50–1.76 (6 H, m), 1.83–1.97 (2 H, m), 2.73 (1 H, tt, *J* = 7.5, 7.5), 3.74 (2 H, s), 5.49 (1 H, br s), 6.80 (2 H, d, *J* = 8.0), 7.10 (2 H, d, *J* = 8.0);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 25.1, 30.0, 33.0, 51.3, 80.2, 101.3, 115.5, 125.2, 130.9, 154.9, 186.6; HRMS (ESI<sup>+</sup>): Found: 251.1041; C<sub>15</sub>H<sub>16</sub>NaO<sub>2</sub> (MNa<sup>+</sup>) Requires 251.1043 (0.7 ppm error).

**4-CyclopentyIspiro[4.5]deca-3,6,9-triene-2,8-dione** (10r). Synthesised using general procedure C2 from ynone **11r** (60.2 mg, 0.264 mmol) and AgNO<sub>3</sub>·SiO<sub>2</sub> (448 mg, 0.0264 mmol) for 6 h at RT. Afforded the *title compound* **10r** without further purification as a white solid (60.0 mg, 100%); mp 129–131 °C; R<sub>f</sub> 0.43 (1:1 hexane:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 2958, 1697, 1657, 1621, 1609, 1403, 1249, 864; δ<sub>H</sub> (400 MHz, CDCI<sub>3</sub>) 1.37–1.50 (2 H, m), 1.52–1.67 (2 H, m), 1.68–1.82 (2 H, m), 1.83–1.95 (2 H, m), 2.30 (1 H, tt, *J* = 8.0, 8.0), 2.64 (2 H, s), 6.22 (1 H, s), 6.44 (2 H, d, *J* = 10.0), 6.69 (2 H, d, *J* = 10.0); δ<sub>C</sub> (100 MHz, CDCI<sub>3</sub>) 25.5, 34.8, 40.2, 45.0, 53.0, 129.0, 130.5, 150.0, 185.0, 186.8, 204.7; HRMS (ESI<sup>+</sup>): Found: 251.1033; C<sub>15</sub>H<sub>16</sub>NaO<sub>2</sub> (MNa<sup>+</sup>) Requires 251.1043 (3.9 ppm error). Found: 229.1215; C<sub>15</sub>H<sub>17</sub>O<sub>2</sub> (MH<sup>+</sup>) Requires 229.1223 (3.7 ppm error).

2-(2-Hydroxyphenyl)-N-methoxy-N-methylacetamide (S5). Synthesised using general procedure A2 from 2-(2hydroxyphenyl)acetic acid (2.00 g, 13.1 mmol) stirring at RT for 1.5 h. Purification by flash column chromatography (9:1 hexane:EtOAc, then 1:1 hexane:EtOAc) afforded the title compound S5 as a white solid (788 mg, 31%); mp 63-65 °C; R<sub>f</sub> 0.39 (1:1 hexane:EtOAc);  $v_{max}$  (thin film)/cm<sup>-1</sup> 3260, 1628, 1596, 1456, 1246, 1000, 753;  $\delta_{H}$  (400 MHz, CDCl<sub>3</sub>) 3.24 (3 H, s), 3.80 (3 H, s), 3.87 (2 H, s), 6.85 (1 H, dd, J = 8.0, 7.5), 6.99 (1 H, d, J = 8.0), 7.09 (1 H, d, J = 7.5), 7.19 (1 H, dd, J = 8.0, 8.0), 9.50 (1 H, s);  $\delta_{C}$  (100 MHz, CDCl<sub>3</sub>) 32.0, 35.1, 62.0, 118.2, 120.2, 120.9, 129.1, 130.9, 156.8, 173.5; HRMS (ESI<sup>+</sup>): Found: 218.0794; C<sub>10</sub>H<sub>13</sub>NNaO<sub>3</sub> (MNa<sup>+</sup>) Requires 218.0788 (-3.0 ppm error), Found: 196.0967; C<sub>10</sub>H<sub>14</sub>NO<sub>3</sub> (MH<sup>+</sup>) Requires 196.0968 (-0.8 ppm error).

4-Cyclopropyl-1-(2-hydroxyphenyl)but-3-yn-2-one (11s). Synthesised using general procedure Β2 from ethynylcyclopropane (0.65 mL, 7.68 mmol) and Weinreb amide S5 (500 mg, 2.56 mmol) stirring at RT for 45 min. Purification by flash column chromatography (1:1 hexane:EtOAc) afforded the title compound 11s as an off-white solid (452 mg, 88%); mp 98–100 °C;  $R_f$  0.78 (1:1 hexane:EtOAc);  $v_{max}$  (thin film)/cm<sup>-1</sup> 3369, 2202, 1649, 1458, 1269, 755; δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>) 0.87-0.92 (2 H, m), 0.97-1.04 (2 H, m), 1.37-1.45 (1 H, m), 3.85 (2 H, s), 6.70 (1 H, br s), 6.88-6.93 (2 H, m), 7.11 (1 H, app. d, J = 7.5), 7.19 (1 H, app. dd, J = 8.0, 8.0);  $\delta_{c}$  (100 MHz, CDCl<sub>3</sub>) –0.1, 10.2, 47.5, 76.8, 103.2, 117.1, 120.6, 120.9, 129.2, 131.3, 154.9, 187.2; HRMS (ESI<sup>+</sup>): Found: 223.0738; C<sub>13</sub>H<sub>12</sub>NaO<sub>2</sub> (MNa<sup>+</sup>) Requires 223.0730 (-3.6 ppm error), Found: 201.0918;  $C_{13}H_{13}O_2$  (MH<sup>+</sup>) Requires 201.0910 (-3.8 ppm error).

(11t).

(12t).

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201.0910 (1.3 ppm error).

**4-Cyclopropylspiro[4.5]deca-3,7,9-triene-2,6-dione** (12s). So Synthesised using general procedure C2 from ynone **11s** (108 he mg, 0.538 mmol) and AgNO<sub>3</sub>·SiO<sub>2</sub> (915 mg, 0.0538 mmol) for 2 15 h at RT. Afforded the *title compound* **12s** without further (2 purification as a yellow oil (104 mg, 96%); R<sub>f</sub> 0.34 (1:1 7. hexane:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 1694, 1660, 1632, 1607, 11 1557, 1200, 862; δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>) 0.68–0.79 (2 H, m), 16 0.97–1.09 (2 H, m), 1.20–1.28 (1 H, m), 2.39 (1 H, d, *J* = 18.0), (N 2.77 (1 H, d, *J* = 18.0), 5.72 (1 H, s), 6.23 (1 H, d, *J* = 9.5), 6.28 (1 H, d, *J* = 9.0), 6.47 (1 H, dd, *J* = 9.0, 5.5), 7.19 (1 H, ddd, *J* = 9.5, 5.5, 1.5); δ<sub>C</sub> (100 MHz, CDCl<sub>3</sub>) 11.0, 11.9, 13.2, 46.8, 62.7, (1 122.8, 123.9, 126.7, 142.5, 142.8, 184.5, 200.3, 206.2; HRMS (5 (ESI<sup>+</sup>): Found: 223.0732; C<sub>13</sub>H<sub>12</sub>NaO<sub>2</sub> (MNa<sup>+</sup>) Requires 223.0730 fo (–1.3 ppm error), Found: 201.0907; C<sub>13</sub>H<sub>13</sub>O<sub>2</sub> (MH<sup>+</sup>) Requires

#### 1-(2-Hydroxyphenyl)-4-phenylbut-3-yn-2-one

Synthesised using general procedure B2 from phenylacetylene (2.0 mL, 18.1 mmol) and Weinreb amide **S5** (1.18 g, 6.04 mmol) stirring at RT for 1 h. Purification by flash column chromatography (9:1 hexane:EtOAc, then 7:3 hexane:EtOAc) afforded the *title compound* **11t** as a yellow solid (1.33 g, 93%); mp 106–108 °C; R<sub>f</sub> 0.67 (6:4 hexane:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 3333, 2982, 2202, 1661, 1489, 1458, 1156,753;  $\delta_{\rm H}$  (400 MHz, CDCl<sub>3</sub>) 4.01 (2 H, s), 6.27 (1 H, br s), 6.94–6.98 (2 H, m), 7.19–7.26 (2 H, m), 7.39 (2 H, m), 7.45–7.50 (1 H, m), 7.51–7.55 (2 H, m);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 47.5, 87.8, 94.0, 116.8, 119.6, 120.4, 121.0, 128.6, 129.3, 131.1, 131.5, 133.3, 154.8, 187.0; HRMS (ESI<sup>+</sup>): Found: 259.0722; C<sub>16</sub>H<sub>12</sub>NaO<sub>2</sub> (MNa<sup>+</sup>) Requires 259.0730 (3.1 ppm error), Found: 237.0914; C<sub>16</sub>H<sub>13</sub>O<sub>2</sub> (MH<sup>+</sup>) Requires 237.0910 (–1.5 ppm error).

#### 4-Phenylspiro[4.5]deca-3,7,9-triene-2,6-dione

Synthesised using general procedure C2 from ynone **11t** (115 mg, 0.487 mmol) and AgNO<sub>3</sub>·SiO<sub>2</sub> (826 mg, 0.0487 mmol) for 24 h at RT. Purification by flash column chromatography (9:1 hexane:EtOAc, then 1:1 hexane:EtOAc) afforded the *title compound* **12t** a pale yellow oil (103 mg, 90%); R<sub>f</sub> 0.22 (7:3 hexane:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 1694, 1659, 1595, 1195, 760;  $\delta_{\rm H}$  (400 MHz, CDCl<sub>3</sub>) 2.54 (1 H, d, *J* = 18.0), 2.78 (1 H, d, *J* = 18.0), 6.34 (1 H, d, *J* = 10.0), 6.44–6.49 (2 H, m), 6.77 (1 H, s), 7.24–7.30 (1 H, m), 7.30–7.38 (4 H, m), 7.38–7.44 (1 H, m);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 48.3, 60.5, 121.8, 126.5, 127.3, 129.0, 129.5, 131.5, 132.3, 142.3, 144.6, 173.7, 200.2, 204.6; HRMS (ESI<sup>+</sup>): Found: 259.0723; C<sub>16</sub>H<sub>12</sub>NaO<sub>2</sub> (MNa<sup>+</sup>) Requires 259.0730 (2.5 ppm error), Found: 237.0906; C<sub>16</sub>H<sub>13</sub>O<sub>2</sub> (MH<sup>+</sup>) Requires 237.0910 (1.9 ppm error).

The *title compound* was also prepared in an enantioenriched form using CPA **16**<sup>15</sup> (56% conv., 23% *ee*, see Scheme 4);  $[\alpha]_{D}^{21}$  = +5.6 (c = 0.2, CHCl<sub>3</sub>).

#### 1-(2-Hydroxyphenyl)-4-(4-methoxyphenyl)but-3-yn-2-one

(11u). Synthesised using general procedure B2 from 1-ethynyl-4-methoxybenzene (1.01 g, 7.68 mmol) and Weinreb amide **S5** (500 mg, 2.56 mmol) stirring at RT for 1 h. Purification by flash column chromatography (9:1 hexane:EtOAc, then 7:3 hexane:EtOAc) afforded the *title compound* **11u** as a yellow solid (478 mg, 70%); mp 108–110 °C; R<sub>f</sub> 0.29 (7:3 hexane:EtOAc);  $v_{max}$  (thin film)/cm<sup>-1</sup> 3364, 2193, 1645, 1599, 1508, 1254, 1080, 834;  $\delta_{H}$  (400 MHz, CDCl<sub>3</sub>) 3.85 (3 H, s), 3.99 (2 H, s), 6.64 (1 H, s), 6.87–6.96 (4 H, m), 7.17–7.24 (2 H, m), 7.49 (2 H, d, *J* = 8.0);  $\delta_{C}$  (100 MHz, CDCl<sub>3</sub>) 47.6, 55.4, 87.0, 95.8, 111.2, 114.4, 117.1, 120.7, 121., 129.2, 131.5, 135.5, 154.9, 162.0, 187.2; HRMS (ESI<sup>+</sup>): Found: 289.0833; C<sub>17</sub>H<sub>14</sub>NaO<sub>3</sub> (MNa<sup>+</sup>) Requires 289.0835 (0.6 ppm error).

DOI: 10.1039/C6OB02426B

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#### 4-(4-Methoxyphenyl)spiro[4.5]deca-3,7,9-triene-2,6-dione

(12u). Synthesised using general procedure C2 from ynone 11u (50 mg, 0.188 mmol) and AgNO<sub>3</sub>·SiO<sub>2</sub> (319 mg, 0.0188 mmol) for 24 h at RT. Afforded the *title compound* 12u without further purification as a yellow oil (49.5 mg, 99%); R<sub>f</sub> 0.25 (1:1 hexane:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 1689, 1659, 1602, 1587, 1510, 1262, 1179, 1026, 833, 731;  $\delta_{\rm H}$  (400 MHz, CDCl<sub>3</sub>) 2.51 (1 H, d, *J* = 18.0), 2.75 (1 H, d, *J* = 18.0), 3.81 (3 H, s), 6.34 (1 H, d, *J* = 9.5), 6.45–6.47 (2 H, m), 6.68 (1 H, s), 6.85 (2 H, d, *J* = 8.5), 7.25–7.31 (3 H, m);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 48.3, 55.4, 60.4, 114.4, 121.5, 124.8, 126.5, 127.2, 129.2, 142.3, 145.0, 162.2, 173.4, 200.5, 204.5; HRMS (ESI<sup>+</sup>): Found: 289.0834; C<sub>17</sub>H<sub>14</sub>NaO<sub>3</sub> (MNa<sup>+</sup>) Requires 289.0835 (0.4 ppm error), Found: 267.1004; C<sub>17</sub>H<sub>15</sub>O<sub>3</sub> (MH<sup>+</sup>) Requires 267.1016 (4.2 ppm error).

#### 4-(4-Fluorophenyl)-1-(2-hydroxyphenyl)but-3-yn-2-one (11v).

Synthesised using general procedure B2 from 1-ethynyl-4-fluorobenzene (923 mg, 7.68 mmol) and Weinreb amide **S5** (500 mg, 2.56 mmol) stirring at RT for 1 h. Purification by flash column chromatography (9:1 hexane:EtOAc, then 7:3 hexane:EtOAc) afforded the *title compound* **11v** as a yellow solid (430 mg, 66%); mp 115–117 °C; R<sub>f</sub> 0.46 (7:3 hexane:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 3357, 2203, 1651, 1598, 1505, 1458, 1234, 1082, 838, 754;  $\delta_{\rm H}$  (400 MHz, CDCl<sub>3</sub>) 3.99 (2 H, s), 6.25 (1 H, s), 6.89–6.97 (2 H, m), 7.08 (2 H, dd, <sup>3</sup>J<sub>HH</sub> = 8.5, <sup>3</sup>J<sub>HF</sub> 8.5), 7.18–7.25 (2 H, m), 7.51 (2 H, dd, <sup>3</sup>J<sub>HH</sub> = 8.5, <sup>4</sup>J<sub>HF</sub> = 5.5);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 47.4, 87.7, 92.8, 115.7 (d, <sup>4</sup>J<sub>CF</sub> = 4.0), 116.2 (d, <sup>2</sup>J<sub>CF</sub> = 22.0), 116.8, 120.4, 121.1, 129.3, 131.5, 135.6 (d, <sup>3</sup>J<sub>CF</sub> = 8.5), 154.7, 164.1 (d, <sup>1</sup>J<sub>CF</sub> = 255), 186.8; HRMS (ESI<sup>+</sup>): Found: 277.0628; C<sub>16</sub>H<sub>11</sub>FNaO<sub>2</sub> (MNa<sup>+</sup>) Requires 277.0635 (2.5 ppm error).

#### 4-(4-Fluorophenyl)spiro[4.5]deca-3,7,9-triene-2,6-dione

**(12v).** Synthesised using general procedure C2 from ynone **11v** (98.8 mg, 0.389 mmol) and AgNO<sub>3</sub>·SiO<sub>2</sub> (661 mg, 0.0389 mmol) for 48 h at RT. Purification by flash column chromatography (8:2 EtOAc:hexane) afforded the *title compound* **12v** a yellow oil (88.7 mg, 90%); R<sub>f</sub> 0.36 (1:1 hexane:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 1694, 1659, 1601, 1582, 1508, 1238, 1193, 1163, 836;  $\delta_{\rm H}$  (400 MHz, CDCl<sub>3</sub>) 2.53 (1 H, d, *J* = 18.0), 2.76 (1 H, d, *J* = 18.0), 6.33 (1 H, d, *J* = 9.5), 6.42–6.50 (2 H, m), 6.70 (1 H, s), 7.03 (2 H, dd, <sup>3</sup>*J*<sub>HH</sub> = 8.5, <sup>3</sup>*J*<sub>HF</sub> 8.5), 7.25–7.29 (1 H, m), 7.29–7.34 (2 H, m);  $\delta_{\rm C}$  (100 MHz, CDCl<sub>3</sub>) 48.4, 60.5, 116.2 (d, <sup>2</sup>*J*<sub>CF</sub> = 22.0), 121.9, 126.5, 128.6 (d, <sup>4</sup>*J*<sub>CF</sub> = 3.0), 129.2, 129.5 (d, <sup>3</sup>*J*<sub>CF</sub> = 8.5), 142.4, 144.3, 164.3 (d, <sup>1</sup>*J*<sub>CF</sub> = 254), 172.3, 200.1, 204.3; HRMS (ESI<sup>+</sup>): Found: 277.0642; C<sub>16</sub>H<sub>11</sub>FNaO<sub>2</sub> (MNa<sup>+</sup>) Requires 277.0635 (-2.4 ppm error), Found: 255.0818; C<sub>16</sub>H<sub>12</sub>FO<sub>2</sub> (MH<sup>+</sup>) Requires 255.0816 (-0.7 ppm error).

Published on 23 November 2016. Downloaded by Athabasca University on 23/11/2016 12:57:49

DOI: 10.1039/C6OB02426B

tert-Butvl 3-(4-(4-hydroxyphenyl)-3-oxobut-1-yn-1-yl)-1Hindole-1-carboxylate (13). Synthesised using general procedure B2 from *tert*-butyl 3-ethynyl-1H-indole-1carboxylate<sup>5</sup> (738 mg, 3.06 mmol) and Weinreb amide **S3** (199 mg, 1.02 mmol) stirring at RT for 1 h. Purification by flash column chromatography (9:1 hexane:EtOAc, then 8:2 hexane:EtOAc) afforded the title compound 13 as a yellow oil (306 mg, 80%); R<sub>f</sub> 0.37 (7:3 hexane:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 3374, 2980, 2188, 1743, 1369, 1232, 1150, 1072;  $\delta_{\rm H}$  (400 MHz, CDCl<sub>3</sub>) 1.70 (9 H, s), 3.89 (2 H, s), 4.98 (1 H, br s), 6.87 (2 H, d, J = 8.0), 7.23 (2 H, d, J = 8.0), 7.32 (1 H, dd, J = 8.0, 7.5), 7.38 (1 H, dd, J = 8.0, 7.5), 7.51 (1 H, d, J = 8.0), 7.91 (1 H, s), 8.14 (1 H, d, J = 8.0);  $\delta_{C}$  (100 MHz, CDCl<sub>3</sub>) 28.2, 51.2, 85.3, 86.8, 92.4, 100.5, 115.5, 115.8, 120.1, 123.8, 125.7, 125.8, 129.9, 131.2, 133.1, 134.8, 148.6, 155.2, 185.3; HRMS (ESI<sup>+</sup>): Found: 398.1357; C<sub>23</sub>H<sub>21</sub>NNaO<sub>4</sub> (MNa<sup>+</sup>) Requires 398.1363 (1.5 ppm error). Note: some peaks broadened in <sup>13</sup>C NMR spectrum due to presence of rotamers.

tert-Butyl3-(3-0x0-5-(4-0x0cyclohexa-2,5-dien-1-yl)cyclopent-1-en-1-yl)-1H-indole-1-carboxylate(8).Synthesised using general procedure C2 from ynone 13 (68.4 mg, 0.182 mmol) and AgNO<sub>3</sub>·SiO<sub>2</sub> (310 mg, 0.0182 mmol) for 7

h at RT. Afforded the *title compound* **8** without further purification as a pale brown solid (67.9 mg, 99%); mp 190–192 °C; R<sub>f</sub> 0.46 (1:1 hexane:EtOAc); v<sub>max</sub> (thin film)/cm<sup>-1</sup> 1742, 1694, 1662, 1595, 1370, 1351, 1228, 1148, 1109, 861, 732; δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>) 1.63 (9 H, s), 2.76 (2 H, s), 6.50 (2 H, d, *J* = 9.5), 6.91 (1 H, s), 6.97 (2 H, d, *J* = 9.5), 7.34–7.45 (2 H, m), 7.78 (1 H, d, *J* = 8.0), 7.93 (1 H, s), 8.25 (1 H, d, *J* = 8.0); δ<sub>C</sub> (100 MHz, CDCl<sub>3</sub>) 28.0, 45.6, 51.9, 85.4, 114., 115.7, 120.3, 124.2, 125.7, 127.8, 128.2, 128.4, 129.7, 135.8, 148.4, 151.9, 165.9, 184.3, 203.4. Note: some peaks broadened in <sup>13</sup>C NMR spectrum due to presence of rotamers. Spectroscopic data matched those previously reported in the literature.<sup>5</sup>

#### 5-methyl-4a,5,6,7-tetrahydrocyclopenta[d]quinoline-

**3,9(4H,10H)-dione(14).** To a stirred solution of *tert*-butyl (2-(3,8-dioxospiro[4.5]deca-1,6,9-trien-1-

yl)ethyl)(methyl)carbamate 10o (64.2 mg, 0.202 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (2 mL) at 0 °C was added TFA (0.2 mL) dropwise. The mixture was warmed to RT and stirred for 2 h. The reaction was quenched by the addition of sat. aq. NaHCO<sub>3</sub> (5 mL). The organic layer was separated and the aqueous layer extracted with  $CH_2Cl_2$  (2 × 5 mL). The organics were combined, washed with brine, dried over MgSO4 and concentrated in vacuo. The crude material was purified by flash column chromatography (9:1 EtOAc:MeOH) to afford the title compound 14 as a colourless oil (29.2 mg, 66%); R<sub>f</sub> 0.47 (9:1 EtOAc:MeOH); v<sub>max</sub> (thin film)/cm  $^{\text{-1}}$  2790, 1709, 1684, 1632, 1209;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 2.23-2.32 (4 H, m), 2.45-2.54 (2 H, m), 2.58-2.75 (4 H, m), 2.87 (1 H, dd, J = 16.0, 2.5), 3.10 (1 H, ddd, J = 11.0, 5.5, 2.5), 6.00 (1 H, s), 6.09 (1 H, d, J = 10.0), 6.41 (1 H, dd, J = 10.0, 2.5); δ<sub>c</sub> (100 MHz, CDCl<sub>3</sub>) 29.7, 40.0, 42.1, 45.9, 49.4, 56.7, 70.2, 127.7, 129.2, 149.8, 181.3, 196.1, 204.9; HRMS (ESI<sup>+</sup>): Found: 218.1170;  $C_{13}H_{16}NO_2$  (MH<sup>+</sup>) Requires 218.1176 (2.5 ppm error).

#### 4,4a,6,7-Tetrahydro-3H-cyclopenta[d]chromene-3,9(10H)-

dione (15). To a 10 mL reaction vial containing 4-(2-((tertbutyldimethylsilyl)oxy)ethyl)spiro[4.5]deca-3,6,9-triene-2,8dione 10p (31.0 mg, 0.097 mmol) in THF (3 mL) was added 10% aqueous HCl (0.1 mL) and the reaction stirred under argon at RT. After 1.5 h, the reaction was quenched with saturated aqueous NaHCO<sub>3</sub> (10 mL), extracted successively with EtOAc (3 x 10 mL), the combined organics washed with brine (10 mL), dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated to yield a crude product. The product was purified by flash column chromatography (8:2 hexane:EtOAc, then 8:2 EtOAc:hexane) to afford the title compound 15 as an off-white solid (15.0 mg, 75%); R<sub>f</sub> 0.47 (EtOAc); mp 115–120 °C; v<sub>max</sub> (thin film)/cm<sup>-1</sup> 3564, 2961, 2925, 2856, 1706, 1682, 1629, 1404, 1234, 1204, 1060, 1009, 781, 701;  $\delta_{H}$  (400 MHz, CDCl<sub>3</sub>) 2.40 (1 H, d, J = 18.5), 2.55 (1 H, d, J = 18.5), 2.60–2.75 (4 H, m), 3.50 (1 H, dt, J = 11.5, 3.0), 3.81-3.83 (1 H, m), 4.22 (1 H, ddd, J = 11.5, 5.5, 2.5), 6.08 (1 H, d, J = 1.5), 6.13 (1 H, d, J = 10.0), 6.42 (1 H, dd, J = 10.0, 3.0);  $\delta_{C}$ (100 MHz, CDCl<sub>3</sub>) 30.1, 41.5, 44.3, 48.9, 68.1, 81.5, 128.8, 129.7, 148.2, 179.5, 195.1, 204.3; HRMS (ESI<sup>+</sup>): Found: 227.0680;  $C_{12}H_{12}NaO_3$  (MNa<sup>+</sup>) Requires 227.0679 (-0.6 ppm error).

#### Acknowledgements

The authors would like to thank the University of York (A.K.C., J.D.C., W.P.U.), the EPSRC (J.T.R.L. EP/M018601/01) and the Leverhulme Trust (for an Early Career Fellowship, ECF-2015-013, W.P.U.) for financial support. We would also like to thank Jack Partington, Harry Kirby, Jamie Rose and Richard Bickford-Smith (University of York undergraduate students) for assistance during preliminary studies.

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