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Nora Dittrich, Eun-Kyung Jung, Samuel J. Davidson, David Barker

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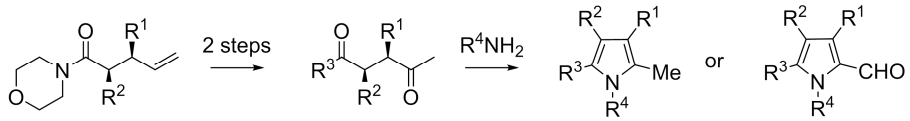
Nora Dittrich, Eun-Kyung Jung, Samuel J. Davidson, David Barker*
School of Chemical Sciences, University of Auckland, 23 Symonds St, Auckland, New Zealand



An acyl-Claisen/Paal-Knorr approach to fully substituted pyrroles.

Nora Dittrich, Eun-Kyung Jung, Samuel J. Davidson, David Barker*

School of Chemical Sciences, University of Auckland, 23 Symonds St, Auckland, New Zealand

*Corresponding author. Tel.: +64-9-373-7599; fax: +64-64-373-7422; e-mail: d.barker@auckland.ac.nz

Abstract: The synthesis of fully substituted pyrroles using the Paal-Knorr reaction on acyl-Claisen derived 2,3-*syn*-disubstituted-1,4-diketones is reported. The use of the acyl-Claisen rearrangement allows the synthesis of wide variety of *syn*-substituted 1,4-diketones which are shown to be better substrates for pyrrole condensation than their corresponding *anti* isomers. When the reaction was performed open to air the use of nucleophilic amines in the pyrrole forming step leads to auto-oxidation of the 5-methyl group giving exclusively 5-formyl pyrroles.

Keywords: Pyrrole; Paal-Knorr; Acyl-Claisen; Oxidation

1. Introduction

The pyrrole ring features in a number of biologically active molecules with a wide range of pharmacological activities. Compounds containing the pyrrole core have been found to possess antitumoral, antimalarial, antifungal, antibacterial and anti-HIV activity and as such, they represent interesting lead compounds for drug development.[1–6] The pharmaceutical potential of pyrrolic compounds is exemplified by the HMG-CoA reductase inhibitor atorvastatin, which has become one of the best-selling pharmaceutical products since its introduction to the global market in 1990.[7–9] Pyrrolic compounds continue to enter the pharmaceutical market and include molecules such as the receptor tyrosine kinase inhibitor sunitinib, approved in 2011 for the treatment of advanced neuroendocrine tumours of the pancreas.[7,10,11] Pyrroles also feature in a number of molecules presently undergoing preclinical trials such as lamellarin D, which is being investigated for its anticancer activity (Figure 1).[12]

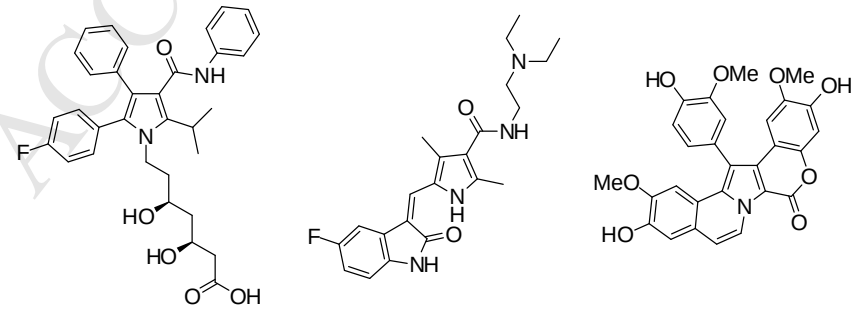


Figure 1: Pyrrolic pharmaceutical compounds

The synthesis of pyrroles can be achieved by a variety of reactions including the well documented Paal-Knorr condensation, first reported in 1884.[13] Despite the successful synthesis of pyrroles through this reaction a major limitation is introduced through the preparation of racemic diketone precursors for the condensation to form the

pyrrole core. Although stereochemistry is lost in the condensation process, studies by Amarnath *et al.* have shown the kinetics of the reaction are influenced by the stereochemistry of the starting material (Figure 2).[14] This is particularly the case for diketones where the substituents at C-2 and C-3 are alkyl or aryl groups which do not facilitate the deprotonation at these positions.

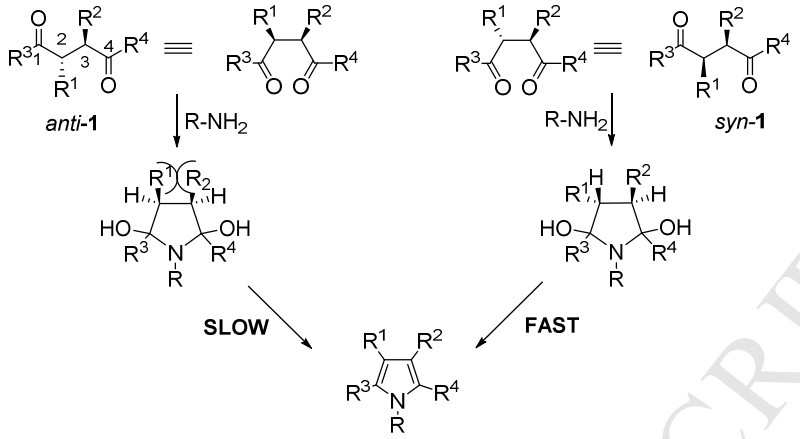


Figure 2: Mechanistic considerations for the Paal-Knorr condensation of *anti* versus *syn*-diketone precursors

1,4-Diketone precursors **1** with *anti*-aligned substituents at C-2 and C-3 adopt an intermediate state which brings these substituents close together, thereby suffering unfavourable steric interactions and reducing the rate of cyclisation. Alternatively, diketones in which these substituents are *syn*-aligned adopt an intermediate state which does not experience these destabilising interactions and therefore condenses to form the pyrrole core occurs faster. With this in mind we envisioned that a diastereoselective synthesis of *syn*-diketones would allow more efficient access to a range of pyrrole compounds.

Our previous work on the acyl-Claisen rearrangement has shown this reaction to be a versatile method for the synthesis of a precursor to these diketones with the desired *syn*-alignment of C2-C3 substituents.[15–19] The reaction involves the *in situ* generation of a ketene from an acid chloride, and the subsequent [3,3] sigmatropic rearrangement of the ketene with an allylic amine yields *syn*-amides in >95% diastereomeric excess over the *anti*-products.[20–22] We therefore proposed that a synthetic route encompassing this reaction could be used to access *syn*-diketones and thus the pyrrole core with high efficiency.

2. Results and Discussion

2.1 Synthesis of *syn*-disubstituted diketones.

We first chose to explore whether the use of *syn*-diketones **1** would indeed lead to higher yielding Paal-Knorr condensations. To this end, two *anti*-diketones were synthesised along with their *syn*-counterparts with the aim of evaluating the effect of stereochemistry on the reaction of these compounds in the Paal-Knorr reaction.

Our synthetic strategy towards *syn*-diketones **1** (Figure 3) involved the synthesis of a range of allylic morpholines and the reaction of these with a variety of acid chlorides using the acyl-Claisen rearrangement. Additional structural diversity could then be introduced by the addition of lithiates to yield ketone products. These would then be converted to their dicarbonyl counterparts *via* the Wacker-Tsuji oxidation and the reaction of these diketones with commercially available amines in the Paal-Knorr reaction would result in a series of pyrroles.

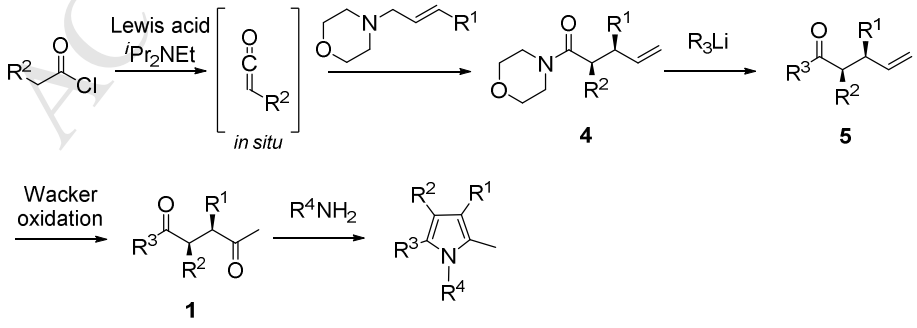
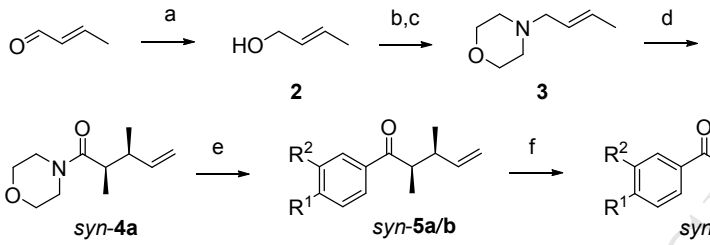


Figure 3: Synthetic strategy.

This short synthetic sequence would in principle allow access to a wide variety of highly substituted and structurally diverse pyrroles with variability at all but the 5-position; bearing a methyl group following pyrrole formation. It was

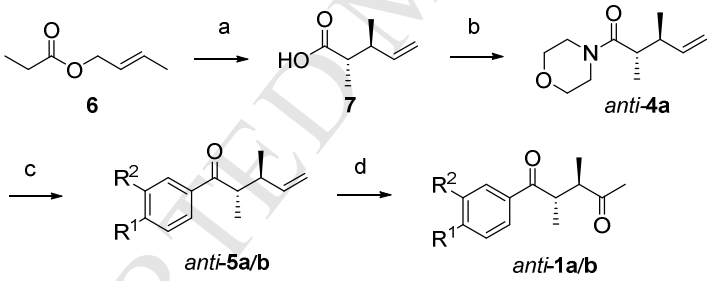
envisaged however that the benzylic nature of this functionality would render it emenable to late stage transformations. To this end various aromatic and aliphatic reactants were selected in order to demonstrate the substrate scope.

Syn-diketones **1a–b** were prepared in six steps as depicted in Scheme 1. Firstly crotonaldehyde was reduced and the resultant (*E*)-alcohol **2** was converted to the corresponding crotyl bromide, which underwent a nucleophilic displacement to give morpholine **3**. Acyl-Claisen rearrangement of amine **3** with propionyl chloride gave morpholine amide **4a** as a single diastereomer in excellent yield. Addition of two different aryl lithiates, gave ketone **5a–b**, which was then followed by a Wacker-Tsuji oxidation to afford the desired *syn*-diketones **1a–b**.



Scheme 1: Synthesis of *syn*-diketones **1a–b**. *Reagents and conditions*: a) $LiAlH_4$, Et_2O, 24 h, 70%; b) PBr_3, Et_2O, 0 °C, 24 h; c) morpholine, NEt_3, CH_2Cl_2, 0 °C to rt, 24 h, 48% over two steps; d) propionyl chloride, $^iPr_2NEt$, $AlCl_3$, CH_2Cl_2, 24 h; 82% e) ^{n}BuLi, 4-bromoanisole or 3,4-methylenedioxybromobenzene, THF, -78 °C to rt, 24 h, **5a** (R^1 = OMe, R^2 = H) 96%, **5b** ($R^1 = R^2$ = -OCH_2O-) 49%; f) $PdCl_2$, CuCl, DMF/H_2O (3:1), O_2, 24 h, **1a** (R^1 = OMe, R^2 = H) 91%, **1b** ($R^1 = R^2$ = -OCH_2O-) 28%.

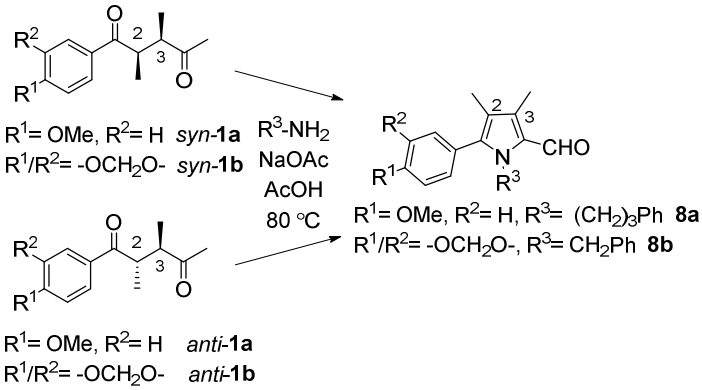
The synthesis of the corresponding *anti*-diketones began with the Ireland-Claisen rearrangement of allylic ester **6** (Scheme 2) giving *anti*-acid **7** which was then coupled with moprholine to give *anti*-morpholine amide **4a**. The remainder of the synthesis was analogous to that of the *syn*-diketones, firstly preparing ketones *anti*-**5a–b**, followed by a Wacker-Tsuji oxidation to install the second ketone functionality.



Scheme 2: Synthesis of *anti*-diketones **1a–b**. *Reagents and conditions*: a) LDA, THF -78 °C, 2 h, 94%; b) morpholine, DCC, DMAP, CH_2Cl_2, 0 °C to rt, 3 d, quant.; c) ^{n}BuLi, 4-bromoanisole or 3,4-methylenedioxybromobenzene, THF, -78 °C to rt, 24 h, *anti*-**5a** (R^1 = OMe, R^2 = H) 50%, *anti*-**5b** ($R^1 = R^2$ = -OCH_2O-) 78%; d) $PdCl_2$, CuCl, DMF/H_2O (3:1), O_2, 24 h, *anti*-**1a** (R^1 = OMe, R^2 = H) 49%, *anti*-**1b** ($R^1 = R^2$ = -OCH_2O-) 68%.

The *syn* and *anti*-diketones **1a–b** were then condensed with benzylamine or 3-phenyl propylamine in the Paal-Knorr reaction. As depicted in Table 1, the difference in reactivity for the starting materials was quite pronounced with the *syn*-diketones resulting in cleaner reactions with higher yields of pyrroles.

Table 1: Paal-Knorr condensation of *syn* and *anti*-diketones **1a–b**.



Diketone	Amine	Product	Yield/Result
syn-**1a**	3-phenylpropylamine	**8a**	58%
anti-**1a**	3-phenylpropylamine	-	Complex mixture
syn-**1b**	benzylamine	**8b**	52%
anti-**1b**	benzylamine	**8b**	21%

These reactions not only highlighted the superior yields when using *syn*-diketones in the Paal-Knorr condensation reaction, but unexpectedly resulted in the formation of the auto-oxidised pyrrole products **8a–b**. Intrigued by the isolation of these pyrrole aldehydes we decided to prepare other pyrroles to determine the generality of the oxidation during pyrrole formation. Three allylic morpholines, crotyl **3**, allyl **9** and cinnamyl morpholines **10** were chosen for the acyl-Claisen rearrangement. The acid chlorides chosen for the acyl-Claisen rearrangement were all commercially available, with the exception of 1,3-benzodioxole-5-propanoyl chloride which was prepared from the corresponding acid. Thus, acid chlorides: propionyl chloride, phenylacetyl chloride, valeroyl chloride, acetyl chloride and 1,3-benzodioxole-5-propanoyl chloride were reacted with morpholines **3**,**9–10** in the acyl-Claisen rearrangement using previously reported conditions[16] yielding a range of *syn*-morpholine amides **4a–h** (Table 2). Reactions were not optimised if they gave sufficient material for further study.

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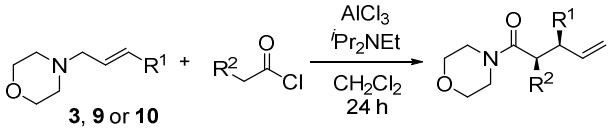
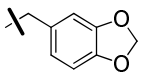
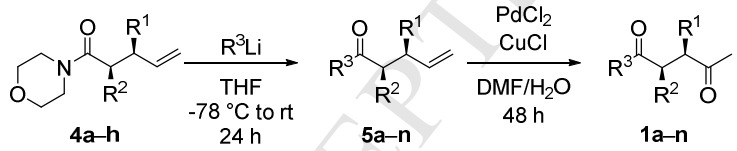
Table 2: Synthesis of 2,3-*syn*-morpholine amides **4a–h**



Allylic Morpholine	R^1	R^2	Product	Yield
3	Me	Me	**4a**	82%
3	Me	Ph	**4b**	86%
3	Me	*n*Pr	**4c**	48%
3	Me		**4d**	Quant.
3	Me	H	**4e**	31%
9	H	Me	**4f**	67%
9	H	Ph	**4g**	49%
10	Ph	Me	**4h**	14%

Either butyllithium or an aryl lithiate (prepared from their corresponding aryl bromides), were then added to the morpholine amides **4a–h** to afford ketones **5a–n** in generally good to excellent yields. The synthesised ketones were then converted to the corresponding diketones **1a-n** using the Wacker-Tsuji oxidations using $PdCl_2$ and CuCl in a DMF/water mixture open to air (Table 3).

Table 3: Synthesis of ketones **5a–n** and diketones **1a–n**



R^1	R^2	R^3	Yield ketone	Yield diketone
Me	Me	4-OMe-Ph	**5a** 96%	**1a** 91%
Me	Me	3,4-OCH_2O-Ph	**5b** 49%	**1b** 80%
Me	Me	3,4-di-OMe-Ph	**5c** 90%	**1c** 98%
Me	Me	3,4,5-tri-OMe-Ph	**5d** 76%	**1d** 86%
Me	Ph	4-OMe-Ph	**5e** 62%	**1e** 72%
Me	Ph	*n*butyl	**5f** 73%	**1f** quant.
Me	*n*Pr	4-OMe-Ph	**5g** 88%	**1g** 55%

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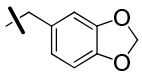
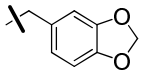
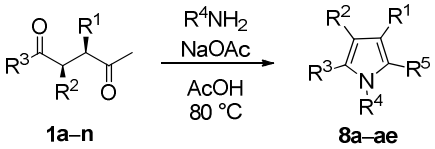
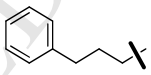
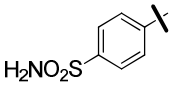
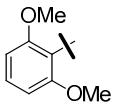
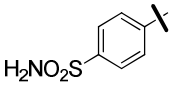
Me		3,4-OCH_2O-Ph	**5h** 28%	**1h** 69%
Me		4-OMe-Ph	**5i** 42%	**1i** 83%
Me	H	3-O^{i}Pr-4-OMe-Ph	**5j** 75%	**1j** 76%
H	Me	4-OMe-Ph	**5k** 99%	**1k** 77%
H	Ph	4-OMe-Ph	**5m** 83%	**1m** 54%
Ph	Me	3,4-OCH_2O-Ph	**5n** 79%	**1n** 96%

The structurally diverse diketones **1a–n** then underwent Paal-Knorr condensation reactions using a series of aliphatic and aromatic amines. Reactions were generally performed open to air but selected reactions were performed under a nitrogen atmosphere (see below). Reactions were carried until complete consumption of diketone (monitored by TLC) and gave a range of pyrrole products **8a–ae** (Table 4).

Table 4: Pyrroles synthesised *via* the Paal-Knorr condensation reaction of diketones **8a–ae**.



1a–n **8a–ae**

Diketone used	R^1	R^2	R^3	R^4	R^5	time (h)	Yield
1a	Me	Me	4-OMe-Ph		CHO	24	**8a** 58%
1a	Me	Me	3,4-OCH_2O-Ph	$PhCH_2$	CHO	4	**8b** 52%
1a	Me	Me	4-OMe-Ph		Me	1	**8c** 65%
1a	Me	Me	4-OMe-Ph	$PhCH_2$	CHO	48	**8d** 26%
1a	Me	Me	4-OMe-Ph	^{n}butyl	CHO	7	**8e** 34%
1b	Me	Me	4-OMe-Ph	Ph	Me	17	**8f** 72%
1b	Me	Me	3,4-OCH_2O-Ph		CHO	48	**8g** 30%[a]
1c	Me	Me	3,4-OMe-Ph	Ph	Me	24	**8h** 25%
1c	Me	Me	3,4-OMe-Ph		Me	24	**8i** 74%[a]

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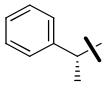
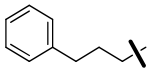
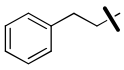
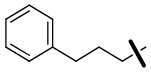
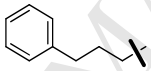
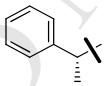
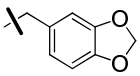
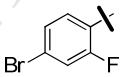
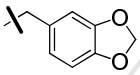
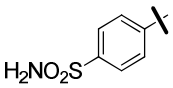
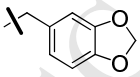
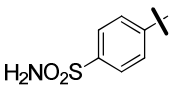
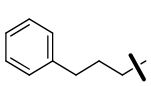
1c	Me	Me	3,4-OMe-Ph	$PhCH_2$	CHO	24	**8j** 48%
1c	Me	Me	3,4-OMe-Ph		CHO	48	**8k** 26%
1c	Me	Me	3,4-OMe-Ph		CHO	48	**8m** 25%
1d	Me	Me	3,4,5-OMe-Ph	3-OTBDPS-4-OMe-Ph	Me	18	**8n** 13%
1d	Me	Me	3,4,5-OMe-Ph	3-OTBDPS-4-OMe-Ph	Me	18	**8n** 74%[b]
1e	Me	Ph	4-OMe-Ph	Ph	Me	24	**8o** 61%
1e	Me	Ph	4-OMe-Ph	$PhCH_2$	Me	24	**8p** 39%[b]
1e	Me	Ph	4-OMe-Ph		CHO	48	**8q** 43%
1e	Me	Ph	4-OMe-Ph		CHO	48	**8r** 55%
1f	Me	Ph	^{n}butyl	Ph	Me	24	**8s** 71%
1f	Me	Ph	^{n}butyl		CHO	24	**8t** 44%
1g	Me	*n*Pr	4-OMe-Ph		CHO	24	**8u** 30%
1h	Me		3,4-OCH_2O-Ph		Me	24	**8v** 24%
1h	Me		3,4-OCH_2O-Ph		Me	24	**8w** 15%
1i	Me		4-OMe-Ph		Me	24	**8x** 29%
1j	Me	H	3-O^{i}Pr-4-OMe-Ph	4-OMe-$PhCH_2$	Me	18	**8y** 59%[b]
1j	Me	H	3-O^{i}Pr-4-OMe-Ph	4-OMe-Ph	Me	18	**8z** 41%[b]
1j	Me	H	3-O^{i}Pr-4-OMe-Ph	$PhCH_2$	Me	18	**8aa** 30%[b]
1k	H	Me	4-OMe-Ph	Ph	Me	24	**8ab** 30%
1k	H	Me	4-OMe-Ph		CHO	72	**8ac** 13%

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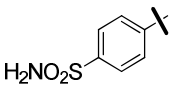
1m	H	Ph	4-OMe-Ph	Ph	Me	24	**8ad** 30%
1n	Ph	Me	3,4-OCH_2O-Ph		Me	24	**8ae** 82%[a]

[a] Yield based on recovered starting material

[b] Reactions conducted under an atmosphere of nitrogen

Diketone precursors with substituents at both C-2 and C-3 (R^2 and R^1) produced pyrroles in higher yields as compared to those with a hydrogen at either one of these positions. It is assumed that the presence of substituents at these positions results in more rapid formation of a cyclic intermediate whilst compounds lacking in substituents have less steric interactions to drive the formation of the cyclic intermediate.

Perhaps more unexpected was the result that the oxidation noted in the earlier Paal-Knorr reactions were also observed in a number of pyrrole products shown in Table 4. A search of the available literature yielded very few examples of auto-oxidation products in pyrrolic compounds. While the oxidation of pyrroles through photo-oxidation reactions is more documented, this generally results in a mixture of products and demands UV irradiation in the presence of an appropriate sensitiser.[23] A report by Schmidt *et al*. detailed the auto-oxidation of the α-methyl group of an *N*-vinyl-2,3-dimethylpyrrole by air, however the pyrrole aldehyde was formed as a minor product. In contrast to this, our reaction conditions often afforded pyrrole aldehyde products exclusively, and in some cases very high yields.

We noted that the amine used appeared to determine the product of the condensation. The more nucleophilic amines such as phenethylamine and 3-phenylpropylamine consistently gave pyrrole aldehydes (eg. **8a**,**e**,**q**) with no unoxidised pyrrole products isolated. In contrast, less nucleophilic amines such as aniline and anilines containing electron withdrawing groups resulted in exclusively unoxidised (i.e. 5-methyl) pyrrole products. Anilines containing alkoxy substituents generally gave mixtures of products where the oxidized pyrrole was the major product. It was discovered that when the reactions of these electron-rich anilines were performed under a nitrogen atmosphere, the unoxidized pyrroles predominated (e.g. **8n**,**z**). The same reactivity was observed with benzylamine and α-methylbenzylamine, where under air 5-formyl pyrroles (**8b,d,j,k,u**) were prepared, whilst under nitrogen unoxidized pyrroles (**8p, aa**) were obtained.

We also observed that reactions leading to pyrrole aldehyde products required longer reaction times. We hypothesised that the 5-methyl pyrroles may represent intermediates in the synthesis of the auto-oxidised formyl pyrrole products. To test this purified 5-methyl pyrroles were stirred under the same conditions for pyrrole formation however this did not result in any oxidation and gave only recovered starting material.

The absence of oxidation products being obtained from 5-methyl pyrroles allowed us to propose that the pyrrole aldehyde products may form due to aerial oxidation of an enamine intermediate, formed by the reaction of the diketone with a nucleophilic amine (Scheme 3). Whilst an enamine intermediate could be formed from all amines we propose that when more nucleophilic amines are employed that the enamine has suitable reactivity to undergo reaction with oxygen, whilst with less nucleophilic amines this reaction is reduced and elimination is preferred. Our observation that reactions performed under a nitrogen atmosphere gave non-oxidized products is in agreement with this proposed mechanism.

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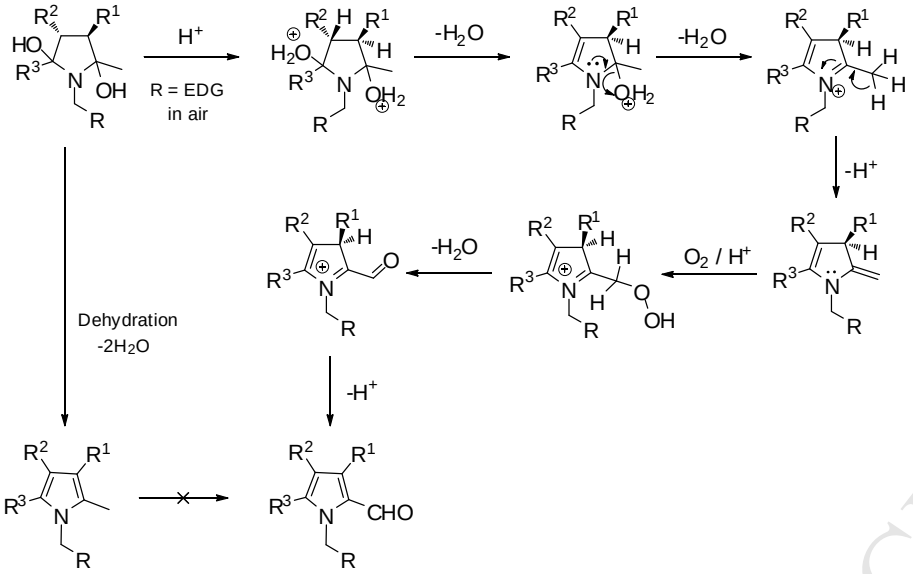

Scheme 3: Proposed mechanism for the auto oxidation of pyrrole products in the Paal-Knorr reaction.

3. Conclusion

In conclusion a range of fully-substituted pyrroles have been prepared from 2,3-*syn*-disubstituted-1,4-diketones under Paal-Knorr conditions. The use of 2,3-*syn* substituted diketones, obtained using an acyl-Claisen rearrangement, is preferential to the corresponding *anti*-diketones or less substituted ketones and results in higher yields of pyrroles. Reactions performed in air with electron rich amines or anilines resulted in oxidation of methyl group to give 5-formyl pyrroles. This result fortuitously allows easy functionalisation of the 5-position of these fully substituted pyrroles, with the other four positions easily modifiable based on the choice of the appropriate starting materials. This auto-oxidation to a 5-formyl group may allow an alternative route to natural products such as lamellarin D which has an ester group at the same position.

4. Experimental section

4.1 General Procedures

All reactions were carried out with oven-dried glassware and under a nitrogen atmosphere in dry, freshly distilled solvents unless otherwise noted. Diisopropylethylamine was distilled from CaH_2 and stored over activated 4Å molecular sieves. Infrared (IR) spectra were recorded using a Perkin Elmer Spectrum1000 FT-IR spectrometer. NMR spectra were recorded on a 300 MHz or 400 MHz spectrometer. Chemical shifts are reported relative to the solvent peak of chloroform (δ 7.26 for ^{1}H and δ 77.16 ± 0.06 for ^{13}C). ^{1}H NMR data is reported as position (δ), relative integral, multiplicity (s, singletl; d, doublet; dd, doublet of doublets; ddd, doublet of doublet of doublets; dt, doublet of triplets; t, triplet; td, triplet of doublets; tt, triplet of triplets; m, multiplet), coupling constant (*J*, Hz), and the assignment of the atom. ^{13}C NMR data are reported as position (δ) and assignment of the atom. NMR assignments were performed using COSY, HSQC and HMBC experiments. High-resolution mass spectroscopy (HRMS) was carried out by either chemical ionisation (CI) or electrospray ionization (ESI) on a MicroTOF-Q mass spectrometer. Unless noted, chemical reagents were used as purchased.

4.2 Synthesis of compounds

4.2.1 General procedure: Acyl-Claisen rearrangement

To a stirred suspension of the Lewis acid (1 mmol) in CH_2Cl_2 (5 mL), under an atmosphere of nitrogen at room temperature, was added dropwise a solution of allyl/crotyl/cinnamyl morpholine (1 mmol) in CH_2Cl_2 (5 mL) dropwise and the resultant suspension stirred for 5 min. DIPEA (1.5 mmol) was added dropwise and the resultant suspension was stirred for a further 15 min. A solution of acid chloride (1.2 mmol) in CH_2Cl_2 (5 mL) was added dropwise and the resultant suspension was stirred for 24 h. A solution of NaOH (1M, 15 mL) was added, the organic layer separated and the aqueous phase further extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried ($MgSO_4$) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography to yield the 2,3-*syn* disubstituted amide product.

4.2.1.1 (2R, 3S*)-2,3-Dimethyl-1-morpholinopent-4-en-1-one syn-**4a***. Flash chromatography using 2:1 hexanes, ethyl acetate to yield 5.0 g, 82% as a pale yellow oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.16. $\boldsymbol{\delta_H}$ (300 MHz; $CDCl_3$; Me_4Si) 1.03 (3H, d, *J* = 6.8 Hz, 3-CH_3), 1.10 (3H, d, *J* = 6.8 Hz, 2-CH_3), 2.48 (1H, sext., *J* = 6.8 Hz, 3-H), 2.57 (1H, pent., *J* = 6.8 Hz, 2-H), 3.51–3.52 and 3.65-3.66 (8H, m, N(CH_2CH_2)$_2$O), 4.95–5.05 (2H, m, 5-H), 5.76 (1H, ddd, *J* = 7.2, 10.3, 17.4 Hz, 4-H). Spectroscopic data were in accordance with literature values.[20]

4.2.1.2 (2S, 3S*)-3-Methyl-1-morpholino-2-phenylpent-4-en-1-one **4b***. Flash chromatography using 2:1 hexanes, ethyl acetate to yield 1.6 g, 86% as a yellow solid. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.33. **MP:** 65–70 °C. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 0.78 (3H, d, *J* = 6.9 Hz, 3-CH_3), 3.05–3.11 (1H, m, 3-H), 3.14–3.19, 3.47–3.70 (9H, m, 2-H, N(CH_2CH_2)$_2$O), 5.01–5.12 (2H, m, 5-H), 5.81–5.90 (1H, m, 4-H), 7.23–7.34 (5H, m, Ar-H). $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 17.3 (3-CH_3), 40.1 (C-3), 42.4, 46.2 (N(CH_2CH_2)$_2$O), 54.2 (C-2), 66.4, 66.8 (N(CH_2CH_2)$_2$O), 114.0 (C-5), 127.1, 128.4, 128.7 (Ar-CH), 138.0 (Ar-C), 142.5 (C-4), 171.0 (C-1). **IR:** ν_{max}(film)/cm^{-1}; 2966, 2853, 1626, 1454, 754, 703. ***m/z*** (ESI^+) 282 (100%), 260 (60), 200 (20), 130 (40). **HRMS** (ESI^+) found (MH^+): 260.1650; $C_{16}H_{22}NO_2$ requires 260.1645.

4.2.1.3 (2R,3S*)-2-Propyl-3-methyl-1-morpholinopent-4-en-1-one **4c***. Flash chromatography using 4:1 hexanes, ethyl acetate to yield 84 mg, 48% as a pale yellow oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.19. $\boldsymbol{\delta_H}$ (300 MHz; CDCl) 0.90 (3H, t, *J* = 6.0 Hz, $CH_2CH_2CH_3$), 1.00 (3H, d, *J* = 6.0 Hz, 3-CH_3), 1.19–1.34 (2H, m, $CH_2CH_2CH_3$), 1.29–1.80 (2H, m, $CH_2CH_2CH_3$), 2.43–2.49 (1H, m, 3-H), 2.57–2.64 (1H, m, 2-H), 3.48–3.67 (8H, m, N(CH_2CH_2)$_2$O), 4.95–5.09 (2H, m, 5-H), 5.65–5.79 (1H, m, 4-H). $\boldsymbol{\delta_C}$ (75 MHz; $CDCl_3$) 14.2 (CH_2CH_3), 16.8 (C-3), 21.0 (CH_2CH_3), 32.0 ($CHCH_2$), 40.3 (C-3), 42.0 (NCH_2), 45.8 (C-2), 46.4 (NCH_2), 66.8 and 67.2 (OCH_2), 114.0 (C-5), 142.0 (C-4), 173.8 (C-1); **IR:** ν_{max}(film)/cm^{-1}; 2961, 2860, 1636, 1435, 1266, 1222, 1116, 1034, 913, 845; ***m/z*** (ESI+) 248 (MNa+, 100 %); **HRMS** (ESI+): found (MH+): 226.1800 $C_{13}H_{24}NO_2$ requires 226.1802.

4.2.1.4 (2R, 3S*)-2-(Benzo[d][1′,3′]dioxol-5′-ylmethyl)-3-methyl-1-morpholinopent-4-en-1-one **4d***. Flash chromatography using 3:1 hexanes, ethyl acetate to yield 0.81 g, quant. as a yellow oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.28. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 1.13 (3H, d, *J* = 7.2 Hz, 3-CH_3), 2.55 (1H, pent., *J* = 7.2 Hz, 3-H), 2.68–2.75 (1H, m, 2-H), 2.78–2.85 (2H, m, 2-CH_2), 2.88–2.95 (1H, m, N(CH_2CH_2)$_2$O), 3.03–3.09 (1H, m, N(CH_2CH_2)$_2$O), 3.19–3.25 (1H, m, N(CH_2CH_2)$_2$O), 3.32–3.39 (2H, m, N(CH_2CH_2)$_2$O), 3.41–3.47 (1H, m, N(CH_2CH_2)$_2$O), 3.55–3.60 (1H, m, N(CH_2CH_2)$_2$O), 3.63–3.68 (1H, m, N(CH_2CH_2)$_2$O), 4.96–5.05 (2H, m, 5-H), 5.72–5.81 (1H, ddd, *J* = 7.6, 10.4, 17.6 Hz, 4-H), 5.90–5.92 (2H, m, 2′-H), 6.60 (1H, dd, *J* = 1.6, 7.8 Hz, 6′-H), 6.50 (1H, d, *J* = 1.6 Hz, 4′-H), 6.69 (1H, d, *J* = 7.8 Hz, 7′-H). $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 17.2 (3-CH_3), 36.4 (2-CH_2), 40.2 (C-3), 41.9, 46.2 (N(CH_2CH_2)$_2$O), 49.0 (C-2), 66.4, 66.9 (N(CH_2CH_2)$_2$O), 100.8 (C-2′), 108.2 (C-7′), 109.5 (C-4′), 114.3 (C-5), 121.9 (C-6′), 133.8 (C-5′), 141.5 (C-4), 145.9 (C-7a′), 147.5 (C-3a′), 172.7 (C-1). **IR:** ν_{max}(film)/cm^{-1}; 2964, 2896, 2857, 1630, 1488, 1441, 1244, 1113, 1036, 926, 809. ***m/z*** (ESI^+) 340 (MNa^+, 100%), 207 (30). **HRMS** (ESI^+) found (MNa^+): 340.1518; $C_{18}H_{23}NNaO_4$ requires 340.1519.

*4.2.1.5 3-Methyl-1-morpholinopent-4-en-1-one **4e***. Flash chromatography using 2:1 hexanes, ethyl acetate to yield 0.39 g, 31% as a pale yellow oil. $\mathbf{R_F}$ = 0.17 (2:1 hexanes, ethyl acetate). $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 1.08 (3H, d, *J* = 6.8 Hz, 3-CH_3), 2.24–2.40 (2H, m, 2-CH_2), 2.70–2.74 (1H, m, 3H), 3.48–3.69 (8H, m, O(CH_2 CH_2)$_2$N), 4.95–5.04 (2H, m, 5-CH_2), 5.77–5.84 (1H, m, 4-H). $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 19.7 (3-CH_3), 34.3 (C-2), 39.4 (C-3), 41.9 (O(CH_2CH_2)$_2$N), 46.1 (O(CH_2CH_2)$_2$N), 66.6 (O(CH_2CH_2)$_2$N), 66.9 (O(CH_2CH_2)$_2$N), 113.1 (C-5), 142.9 (C-4), 170.3 (C-1). **IR**: (film)/cm^{-1}; 3496, 2963, 2922, 1636, 1431, 1226, 1114, 911, 726. ***m/z*** (ESI^+) 206 (MNa^+, 100%). **HRMS** (ESI+) Found (MNa^+): 206.1160; $C_{10}H_{17}NNaO_2$ requires 206.1151.

*4.2.1.6 2-Methyl-1-morpholinopent-4-en-1-one **4f***. Flash chromatography using 2:1 hexanes, ethyl acetate to yield 0.29 g, 67% as a yellow oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.20. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 1.14 (3H, d, *J* = 6.8 Hz, 2-CH_3), 2.13-2.18 (1H, m, 3-H_A), 2.40–2.47 (1H, m, 3-H_B), 2.72 (1H, sext., *J* = 6.8 Hz, 2-H), 3.52–3.53, 3.63–3.69 (8H, m, N(CH_2CH_2)$_2$O), 5.01–5.09 (2H, m, 5-H), 5.71–5.81 (1H, m, 4-H). Spectroscopic data were in accordance with literature values.[20]

*4.2.1.7 1-Morpholino-2-phenylpent-4-en-1-one **4g***. Flash chromatography using 2:1 hexanes, ethyl acetate to yield 0.29 g, 49% as a yellow oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.80**.** $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 2.42–2.49 (1H, m, 3-H_A), 2.83–2.90 (1H, m, 3-H_B), 3.09–3.75 (9H, m, 2-H, N(CH_2CH_2)$_2$O), 5.00–5.05 (2H, m, 5-H), 5.72–5.80 (1H, ddt, *J* = 7.2, 10.0, 17.2 Hz, 4-H), 7.22–7.34 (5H, m, Ar-H). $\boldsymbol{\delta_C}$ (75 MHz; $CDCl_3$) 39.0 (C-3), 42.4, 46.0 (N(CH_2CH_2)$_2$O), 48.9 (C-2), 66.3, 66.7 (N(CH_2CH_2)$_2$O), 116.5 (C-5), 127.1, 127.7, 128.9 (Ar-CH), 136.3 (C-4), 139.4 (Ar-C), 171.0 (C-1). **IR:** ν_{max}(film)/cm^{-1}; 2967, 2919, 1856, 1636, 1454, 1431, 1219, 1113, 751, 700. ***m/z*** (ESI^+) 246 (MH^+, 100), 268 (80). **HRMS** (ESI^+) found (MH^+): 246.1486; $C_{15}H_{20}NO_2$ requires 246.1489.

4.2.1.8 (2R, 3S*)-2-methyl-1-morpholino-3-phenylpent-4-en-1-one **4h***. Flash chromatography using 3:1 hexanes, ethyl acetate to yield 24 mg, 14% as a pale yellow solid. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.29. **MP:** 75–78 °C. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 0.83 (3H, d, *J* = 6.8 Hz, 2-CH_3), 2.98 (1H, dq, *J* = 6.8, 9.8 Hz, 2-H), 3.40–3.56 (9H, m,

$N(CH_2CH_2)_2O$ and 3-H), 4.89–4.98 (2H, m, 5-H), 5.93 (1H, ddd, *J* = 7.8, 10.5, 17.9 Hz, 4-H), 7.09–7.14 (3H, m, Ar-CH), 7.20–7.23 (2H, m, Ar-CH). Spectroscopic data were in accordance with literature values.[20]

4.2.2 General procedure: Lithiate addition of bromides to morpholine amides

A solution of bromide (1.2 mmol) in THF (15 mL) under an atmopshere of nitrogen, was precooled to -78 °C for 5 min. 1.6 M BuLi (2.4 mmol) was added dropwise, and the resultant solution was stirred at -78 °C for 5 minutes prior to the addition of a solution of amide (1 mmol) in THF (15 mL) dropwise. The mixture was stirred for 24 h and allowed to warm to room temperature over this time. Saturated aqueous NH_4Cl solution (20 mL) was added, the organic layer separated and the aqueous phase further extracted with CH_2Cl_2 (3 × 15 mL). The combined organic extracts were dried ($MgSO_4$) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography to yield the ketone product. All ketones **5** have 2,3-*syn* stereochemistry except those formed using amides *anti*-**5a** and *anti*-**5b**.

4.2.2.1 (2R, 3S*)-1-(4′-Methoxyphenyl)-2,3-dimethylpent-4-en-1-one syn-**5a**.* Using amide **4a**. Flash chromatography using 3:1 hexanes, ethyl actetate to yield 0.21 g, 96% as a colourless oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.80. $\boldsymbol{\delta_H}$ (300 MHz; $CDCl_3$; Me_4Si) 0.99 (3H, d, *J* = 6.9 Hz, 3-CH_3), 1.13 (3H, d, *J* = 6.9 Hz, 2-CH_3), 2.64 (1H, sext., *J* = 6.9 Hz, 3-H), 3.41 (1H, pent., *J* = 6.9 Hz, 2-H), 3.87 (3H, s, OCH_3), 4.91–5.04 (2H, m, 5-H), 5.81 (1H, ddd, *J* = 7.1, 10.3, 17.3 Hz, 4-H), 6.94 (2H, d, *J* = 8.8 Hz, 3′′-H), 7.91 (2H, d, *J* = 8.8 Hz, 2′-H). Spectroscopic data were in accordance with literature values.[18]

4.2.2.2 (2S, 3S*)-1-(4′-Methoxyphenyl)-2,3-dimethylpent-4-en-1-one anti-**5a**.* Using amide *anti*-**4a**. Flash chromatography using 2:1 hexanes, ethyl acetate to yield 37 mg, 50% as a yellow oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.72. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 0.99 (3H, d, *J* = 6.8 Hz, 3-CH_3), 1.12 (3H, d, *J* = 6.8 Hz, 2-CH_3), 2.61 (1H, sext., *J* = 6.8 Hz, 3-H), 3.29 (1H, pent., *J* = 6.8 Hz, 2-H), 3.87 (3H, s, OCH_3), 5.00–5.05 (2H, m, 5-H), 5.70 (1H, ddd, *J* = 8.8, 10.0, 18.0 Hz, 4-H), 6.94 (2H, d, *J* = 8.8 Hz, 3′-H), 7.95 (2H, d, *J* = 8.8 Hz, 2′-H). $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 15.6 (2-CH_3), 19.0 (3-CH_3), 41.1 (C-3), 55.4 (C-2), 55.7 (OCH_3), 113.7 (C-3′), 114.8 (C-5), 130.5 (C-1′, C-2′), 141.3 (C-4), 163.4 (C-4′), 202.7 (C-1). **IR:** ν_{max}(film)/cm^{-1}; 2929, 2855, 1672, 1600, 1510, 1453, 1255, 1032. ***m/z*** (ESI^+) 241 (MNa^+, 100%). **HRMS** (ESI^+) found (MNa^+): 241.1203; $C_{14}H_{18}NaO_2$ requires 241.1199.

4.2.2.3 (2R, 3S*)-1-(Benzo[d][1′,3′]dioxol-5′-yl)-2,3-dimethylpent-4-en-1-one syn-**5b**.* Using amide **4a**. Columend using 3:1 hexanes, ethyl acetate to yield 0.57 g, 49% as a yellow oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.74. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 0.99 (3H, d, *J* = 6.8 Hz, 3-CH_3), 1.13 (3H, d, *J* = 7.2 Hz, 2-CH_3), 2.62 (1H, pent., *J* = 6.8 Hz, 3-H), 3.36 (1H, pent., *J* = 6.8 Hz, 2-H), 4.91–5.02 (2H, m, 5-H), 5.79 (1H, ddd, *J* = 7.2, 10.4, 17.2 Hz 4-H), 6.03 (2H, s, 2′-H), 6.86 (1H, d, *J* = 8.4 Hz, 7′-H), 7.42 (1H, d, *J* = 1.6 Hz, 4′-H), 7.54 (1H, dd, *J* = 1.6, 8.4 Hz, 6′-H). $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 13.5 (2-CH_3), 15.6 (3-CH_3), 40.0 (C-3), 45.0 (C-2), 101.8 (C-2′), 107.8 (C-7′), 108.2 (C-4′), 112.3 (C-5), 124.2 (C-6′), 131.9 (C-5′), 142.1 (C-4), 148.2 (C-3a′), 151.5 (C-7a′), 201.8 (C-1). **IR:** ν_{max}(neat)/cm^{-1}; 2972, 2896, 1671, 1605, 1502, 1472, 1438, 800. ***m/z*** (ESI^+) 255 (MNa^+, 100%). **HRMS** (ESI^+) found (MNa^+): 255.1006; $C_{14}H_{16}NaO_3$ requires 255.0992.

4.2.2.4 (2S, 3S*)-1-(Benzo[d][1′,3′]dioxol-5′-yl)-2,3-dimethylpent-4-en-1-one anti-**5b**.* Using amide *anti*-**4a**. Flash chromatography using 2:1 hexanes, ethyl acetate to yield 0.11 g, 78% as a yellow oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.75. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 0.98 (3H, d, *J* = 6.8 Hz, 3-CH_3), 1.11 (3H, d, *J* = 6.8 Hz, 2-CH_3), 2.59 (1H, sext., *J* = 6.8 Hz, 3-H), 3.24 (1H, pent., *J* = 6.8 Hz, 2-H), 5.00–5.05 (2H, m, 5-H), 5.69 (1H, ddd, *J* = 8.4, 9.6, 17.6 Hz, 4-H), 6.02 (2H, s, 2′–H), 6.84 (1H, d, *J* = 8.4 Hz, 7′-H), 7.44 (1H, d, *J* = 1.6 Hz, 4′-H), 7.56 (1H, dd, *J* = 1.6, 8.4 Hz, 6′-H). $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 15.6 (2-CH_3), 18.9 (3-CH_3), 41.1 (C-3), 45.2 (C-2), 101.7 (C-2′), 107.7 (C-7′), 108.0 (C-4′), 114.8 (C-5), 124.2 (C-6′), 132.0 (C-5′), 141.1 (C-4), 148.2 (C-3a′), 151.6 (C-7a′), 202.1 (C-1). **IR:** ν_{max}(film)/cm^{-1}; 2969, 2929, 1670, 1438, 1243, 1037, 810, 741. ***m/z*** (ESI^+) 255 (MNa^+, 100%). **HRMS** (ESI^+) found (MNa^+): 255.1001; $C_{14}H_{16}NaO_3$ requires 255.0992.

4.2.2.5 (2R, 3S*)-1-(3′,4′-Dimethoxyphenyl)-2,3-dimethylpent-4-en-1-one **5c**.* Using amide **4a**. Flash chromatography using 19:1 hexanes, ethyl acetate to yield 0.61 g, 90% as a yellow oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.57. $\boldsymbol{\delta_H}$ (300 MHz; $CDCl_3$; Me_4Si) 1.01 (3H, d, *J* = 6.9 Hz, 2-CH_3), 1.14 (3H, d, *J* = 6.9 Hz, 3-CH_3), 2.65 (1H, sext., *J* = 6.9 Hz, 3-H), 3.46 (1H, pent., *J* = 6.9 Hz, 2-H), 3.94 (3H, s, 3′-OCH_3), 3.95 (3H, s, 4′-OCH_3), 4.92–5.03 (2H, m, 5-H), 5.81 (1H, ddd, *J* = 7.0, 10.1, 17.4 Hz, 4-H), 6.89 (1H, d, *J* = 8.4 Hz, 5′-H), 7.53 (1H, d, *J* = 1.8 Hz, 2′-H), 7.57 (1H, dd, *J* = 1.8, 8.4 Hz, 6′-H). Spectroscopic data were in accordance with literature values.[18,25]

4.2.2.6 (2R,3S*)-2,3-dimethyl-1-(3′,4′,5′-trimethoxyphenyl)pent-4-en-1-one **5d**.* Using amide **4a**. Flash chromatography using 9:1 hexanes, ethyl acetate to yield 0.45 g, 76% as a pale yellow oil. $\mathbf{R_F}$ = 0.71 (2:1, hexanes, ethyl acetate). $\boldsymbol{\delta_H}$ (300 MHz; $CDCl_3$; Me_4Si) 1.01 (3H, d, *J* = 6.8 Hz, 3-CH_3), 1.15 (3H, d, *J* = 6.8 Hz, 2-CH_3), 2.61–2.72 (1H, m, 3-H), 3.36–3.45 (1H, m, 2-H), 3.92 (9H, s, 3′-OCH_3, 4′-OCH_3), 4.93–5.05 (2H, m, 5-CH_2), 5.76–5.87

(1H, m, 4-H), 7.20 (2H, s, 2′-H). **δ_C** (75 MHz; $CDCl_3$) 13.4 (2-CH_3), 15.6 (3-CH_3), 40.1 (C-3), 45.0 (C-2), 56.3 (3′-OCH_3, 4′-OCH_3), 105.8 (C-2′), 114.0 (C-5), 132.2 (C-1′), 142.1 (C-4), 142.5 (C-4′), 153.1 (C-3′), 202.3 (C-1). **IR**: (film)/cm^{-1}; 2976, 2983, 2854, 1674, 1583, 1456, 1413, 1323, 1127, 908, 730. **m/z** (ESI+) 301 (MNa^+, 100%). **HRMS** (ESI+) Found (MNa^+): 301.1403; $C_{16}H_{22}NaO_4$ requires 301.1410.

4.2.2.7 (2S, 3S*)-1-(4′-Methoxyphenyl)-3-methyl-2-phenylpent-4-en-1-one* ***5e***. Using amide **4b**. Flash chromatography using 9:1 hexanes, ethyl acetate to yield 34 mg, 62% as a yellow oil. **R_F** (2:1 hexanes, ethyl acetate) = 0.72. **δ_H** (400 MHz; $CDCl_3$; Me_4Si) 0.84 (3H, d, *J* = 4.0 Hz, 3-CH_3), 3.15–3.23 (1H, m, 3-H), 3.81 (3H, s, OCH_3), 4.35 (1H, d, *J* = 10.2 Hz, 2-H), 4.92–5.09 (2H, m, 5-H), 5.83 (1H, ddd, *J* = 7.0, 10.4, 17.3 Hz, 4-H), 6.86 (2H, d, *J* = 8.9 Hz, 3′-H), 7.18–7.35 (5H, m, Ar-H), 7.95 (2H, d, *J* = 8.9 Hz, 2′-H). **δ_C** (100 MHz; $CDCl_3$) 17.7 (3-CH_3), 40.4 (C-3), 55.4 (OCH_3), 58.9 (C-2), 113.7 (C-3′), 114.3 (C-5), 127.1, 128.7, 128.8 (Ar-CH, C-1′), 130.8 (C-2′), 138.0 (Ar-C), 142.2 (C-4), 163.3 (C-4′), 198.1 (C-1). **IR:** ν_{max}(film)/cm^{-1}; 2961, 1671, 1639, 1598, 1510, 1455, 1261, 1169, 1031, 746, 702. ***m/z*** (ESI^+) 303 (MNa^+, 100%), 281 (30). **HRMS** (ESI^+) found (MNa^+): 303.1360; $C_{19}H_{20}NaO_2$ requires 303.1356.

4.2.2.8 (3S, 4S*)-3-Methyl-4-phenylnon-1-en-5-one* ***5f***. Using amide **4b**. Flash chromatography using 2:1 hexanes, ethyl acetate to yield 32 mg, 73% as a yellow oil. **R_F** (2:1 hexanes, ethyl acetate) = 0.89. **δ_H** (300 MHz; $CDCl_3$; Me_4Si) 0.75–0.81 (6H, m, 3-CH_3, 9-H), 1.07–1.26 (2H, m, 8-H), 1.38–1.50 (2H, m, 7-H), 2.31–2.42 (2H, m, 6-H), 2.96–3.06 (1H, m, 3-H), 3.48 (1H, d, *J* = 9.0 Hz, 4-H), 5.03 (2H, ddd, *J* = 7.4, 10.3, 17.4 Hz, 1-H), 5.72–5.84 (1H, m, 2-H), 7.20–7.33 (5H, m, Ar-H). **δ_C** (75 MHz; $CDCl_3$) 13.7 (C-9), 17.6 (3-CH_3), 22.0 (C-8), 25.4 (C-7), 39.5 (C-3), 42.9 (C-6), 64.8 (C-4), 114.4 (C-1), 127.2, 128.7, 128.9 (Ar-CH), 137.2 (Ar-C), 141.9 (C-2), 209.8 (C-5). **IR:** ν_{max}(neat)/cm^{-1}; 2959, 2932, 2874, 1713, 1641, 1494, 1454, 915, 743. ***m/z*** (ESI^+) 231 (MH^+, 100%), 253 (20). **HRMS** (ESI^+) found (MH^+): 231.1743; $C_{16}H_{23}O$ requires 231.1743.

4.2.2.9 (2R, 3S*)-1-(4'-Methoxyphenyl)-2-propyl-3-methylpent-4-en-1-one* ***5g***. Using amide **4c**. Flash chromatography using 2:1 hexanes, ethyl acetate to yield 81 mg, 88% as a pale yellow oil. **R_F** (2:1 hexanes, ethyl acetate) = 0.82. **δ_H** (400 MHz; $CDCl_3$) 0.92–1.01 (3H, m, 2-$CH_2CH_2CH_3$), 1.00 (3H, d, *J* = 6.9 Hz, 3-CH_3), 1.22–1.31 (4H, m, 2-$CH_2CH_2CH_3$), 2.62 (1H, q, *J* = 6.8 Hz, 2-H), 3.42 (1H, pent., *J* = 6.8 Hz, 3-H), 3.87 (3H, s, OCH_3), 4.91–5.05 (2H, m, 5-H), 5.76–5.87 (1H, m, 4-H), 6.94 (2H, d, *J* = 8.9 Hz, 3′-H), 7.92 (2H, d, *J* = 8.9 Hz, 2′-H). **δ_C** (100 MHz; $CDCl_3$) 14.3 (CH_2CH_3), 16.3 (C-3), 21.1 (CH_2CH_3), 30.9 ($CHCH_2$), 40.1 (C-3), 50.4 (C-2), 55.4 (OCH_3), 113.9 (C-3), 114.0 (C-5), 129.4 (C-2), 131.3 (C-1'), 142.0 (C-4), 163.3 (C-4'), 201.2 (C-1). **IR**: ν_{max}(film)/cm^{-1}; 2958, 2933, 2874, 1671, 1638, 1509, 1462, 1250, 1172, 1032, 913; ***m/z*** (ESI+): 269 (MNa^+, 100%); **HRMS** (ESI+) Found (MNa^+): 269.1508 $C_{16}H_{22}NaO_2$ requires 269.1512.

4.2.2.10 (2R, 3S*)-1-(Benzo[d][1'',3'']dioxol-5''-yl)-2-(benzo[d][1',3']dioxol-5'-ylmethyl)-3-methylpent-4-en-1-one* ***5h***. Using amide **4d**. Flash chromatography using 9:1 hexanes, ethyl acetate to yield 0.12 g, 28% as an orange oil. **R_F** (2:1 hexanes, ethyl acetate) = 0.63. **δ_H** (400 MHz; $CDCl_3$; Me_4Si) 1.04 (3H, d, *J* = 6.8 Hz, 3-CH_3), 2.60 (1H, pent., *J* = 6.8 Hz, 3-H), 2.71 (1H, dd, *J* = 3.7, 13.5 Hz, 2-CH_A), 3.04 (1H, dd, *J* = 10.4, 13.5 Hz, 2-CH_B), 3.56–3.60 (1H, m, 2-H), 4.99–5.07 (2H, m, 5-H), 5.80–5.89 (3H, m, 4-H, 2′-H), 6.00 (2H, s, 2′′-H), 6.56–6.67 (3H, m, 4′-H, 6′-H, 7′-H), 6.76 (1H, d, *J* = 8.1 Hz, 7′′-H), 7.29 (1H, d, *J* = 1.6 Hz, 4′′-H), 7.35 (1H, dd, *J* = 1.6, 8.1 Hz, 6′′-H). **δ_C** (100 MHz; $CDCl_3$) 16.1 (3-CH_3), 33.9 (2-CH_2), 40.2 (C-3), 53.2 (C-2), 100.6 (C-2′), 100.7 (C-2′′), 107.6, 107.7 (C-7′, C-7′′), 108.0 (C-4′′), 109.3 (C-4′), 114.6 (C-5), 121.8 (C-6′), 124.3 (C-6′′), 132.9 (C-5′′), 134.1 (C-5′), 141.2 (C-4), 145.6, 147.3 (C-7a′, C-3a′), 148.0 (C-3a′′), 151.4 (C-7a′′), 200.6 (C-1). **IR:** ν_{max}(film)/cm^{-1}; 2971, 2899, 1667, 1604, 1502, 1486, 1438, 1242, 1035, 925, 808, 733. ***m/z*** (ESI^+) 375 (MNa^+, 40%), 360 (100). **HRMS** (ESI^+) found (MNa^+): 375.1191; $C_{21}H_{20}NaO_5$ requires 375.1203.

4.2.2.11 (2R, 3S*)-2-(Benzo[d][1',3']dioxol-5'-ylmethyl)-1-(4''-methoxyphenyl)-3-methylpent-4-en-1-one* ***5i***. Using amide **4d**. Flash chromatography using 19:1 hexanes, ethyl acetate to yield 0.17 g, 42% as a yellow oil. **R_F** (2:1 hexanes, ethyl acetate) = 0.62. **δ_H** (400 MHz; $CDCl_3$; Me_4Si) 1.04 (3H, d, *J* = 7.0 Hz, 3-CH_3), 2.61 (1H, q, *J* = 7.0 Hz, 3-H), 2.71 (1H, dd, *J* = 3.6, 13.6 Hz, 2-CH_A), 3.06 (1H, dd, *J* = 10.0, 13.6 Hz, 2-CH_B), 3.62–3.67 (1H, m, 2-H), 3.83 (3H, s, OCH_3), 4.91–5.02 (2H, m, 5-H), 5.83–5.91 (3H, m, 4-H, 2′-H), 6.60–6.65 (3H, m, 4′-H, 6′-H, 7′-H), 6.86 (2H, d, *J* = 8.9 Hz, 3′′-H), 7.78 (2H, d, *J* = 8.9 Hz, 2′′-H). **δ_C** (100 MHz; $CDCl_3$) 16.0 (3-CH_3), 33.6 (2-CH_2), 40.1 (C-3), 52.9 (C-2), 55.2 (OCH_3), 100.5 (C-2′), 107.9 (C-7′), 109.3 (C-4′), 113.5, 113.6 (C-3′′), 114.4 (C-5), 121.7 (C-6′), 130.3, 130.4 (C-2′′), 130.9 (C-1′′), 134.2 (C-5′), 141.3 (C-4), 145.5 (C-7a′), 147.3 (C-3a′), 163.1 (C-4′′), 200.9 (C-1). **IR:** ν_{max}(film)/cm^{-1}; 2964, 2910, 2842, 1667, 1597, 1502, 1487, 1441, 1242, 1168, 1035, 919, 803, 732. ***m/z*** (ESI^+) 360 (100), 361 (95). **HRMS** (ESI^+) found (MNa^+): 361.1407; $C_{21}H_{22}NaO_4$ requires 361.1410.

4.2.2.12 1-(3′-isopropoxy-4′-methoxyphenyl)-3-methylpent-4-en-1-one ***5j***. Using amide **4e**. Flash chromatography using 19:1 hexanes, ethyl acetate to yield 0.32 g, 75% as a pale yellow oil. **R_F** = 0.80 (2:1 hexanes, ethyl acetate). **δ_H** (400 MHz; $CDCl_3$; Me_4Si) 1.07 (3H, d, *J* = 6.8 Hz, 3-CH_3), 1.36 (6H, d, *J* = 6.0 Hz, 3′-OCH(CH_3)$_2$), 2.79–2.83 (1H, m, 2-CH_2), 2.85–2.88 (1H, m, 3-H), 2.92–2.97 (1H, m, 2-CH_2), 3.89 (3H, s, 4′-OCH_3), 4.59–4.62 (1H, m, 3′-CH(CH_3)$_2$), 4.92–5.02 (2H, m, 5-H), 5.79–5.86 (1H, m, 4-H), 6.86 (1H, d, *J* = 8.2 Hz, 5′-H) , 7.52 (1H, d, *J* = 2.0 Hz,

2′-H), 7.54 (1H, dd, *J* = 8.2, 2.0 Hz, 6′-H). **δ_C** (100 MHz; $CDCl_3$) 19.8 (3-CH_3), 21.9 (3′-OCH(CH_3)$_2$), 33.9 (C-3), 44.7 (C-2), 56.0 (4′-OCH_3), 71.4 (3′-O*C*H(CH_3)$_2$), 110.6 (C-5′), 112.9 (C-5), 114.4 (C-2′), 122.8 (C-6′), 130.5 (C-1′), 143.4 (C-4), 147.2 (C-3′), 154.5 (C-4′), 197.9 (C-1). **IR**: (film)/cm-1; 2975, 1673, 1592, 1509, 1441, 1266, 1146, 1022, 911, 729. **m/z** (ESI+) 285 (MNa^+, 100%). **HRMS** (ESI+) Found (MNa^+): 285.1469; $C_{16}H_{22}NaO_3$ requires 285.1461.

4.2.2.13 1-(4′-Methoxyphenyl)-2-methylpent-4-en-1-one ***5k***. Using amide **4f**. Flash chromatography using 9:1 hexanes, ethyl acetate to yield 55 mg, 99% as a yellow oil. **R_F** (2:1 hexanes, ethyl acetate) = 0.74. **δ_H** (400 MHz; $CDCl_3$; Me_4Si) 1.19 (3H, d, *J* = 7.2 Hz, 2-CH_3), 2.15–2.23 (1H, m, 3-H_A), 2.51–2.58 (1H, m, 3-H_B), 3.49 (1H, q, *J* = 7.2 Hz, 2-H), 3.86 (3H, s, OCH_3), 4.98–5.07 (2H, m, 5-H), 5.73–5.83 (1H, m, 4-H), 6.94 (2H, d, *J* = 8.8 Hz, 3′-H), 7.95 (2H, d, *J* = 8.8 Hz, 2′-H). Spectroscopic data were in accordance wih literature values.[25]

4.2.2.14 1-(4′-Methoxyphenyl)-2-phenylpent-4-en-1-one ***5m***. Using amide **4g**. Flash chromatography using 14:1 hexanes, ethyl acetate to yield 0.18 g, 83% as a colourless oil. **R_F** (2:1 hexanes, ethyl acetate) = 0.89. **δ_H** (400 MHz; $CDCl_3$; Me_4Si) 2.55 (1H, pent., *J* = 7.2 Hz, 3-H_A), 2.95 (1H, pent., *J* = 7.2 Hz, 3-H_B), 3.70 (3H, s, OCH_3), 4.58 (1H, t, *J* = 7.2 Hz, 2-H), 4.93–5.05 (2H, m, 5-H), 5.70–5.80 (1H, m, 4-H), 6.81 (2H, d, *J* = 8.9 Hz, 3′-H), 7.23–7.34 (5H, m, Ar-H), 7.94 (2H, d, *J* = 8.9 Hz, 2′-H). **δ_C** (100 MHz; $CDCl_3$) 38.0 (C-3), 53.0 (C-2), 55.2 (OCH_3), 113.5 (C-3′), 116.4 (C-5), 126.8, 128.0, 128.7 (Ar-CH), 129.4 (C-1′), 130.8 (C-2′), 136.0 (C-4), 139.3 (Ar-C), 163.2 (C-4′), 197.6 (C-1). **IR:** ν_{max}(film)/cm^{-1}; 3064, 2936, 2839, 1670, 1641, 1510, 1489, 1245, 1029, 824, 700. ***m/z*** (ESI^+) 289 (MNa^+, 100%). **HRMS** (ESI^+) found (MNa^+): 289.1167; $C_{18}H_{18}NaO_2$ requires 289.1199.

4.2.2.15 (2R, 3S*)-1-(Benzo[d][1′,3′]dioxol-5′-yl)-2-methyl-3-phenylpent-4-en-1-one* ***5n***. Using amide **4h**. Flash chromatography using 19:1 hexanes, ethyl acetate to yield 365 mg, 79% as a yellow oil. **R_F** (2:1 hexanes, ethyl acetate) = 0.77. **δ_H** (300 MHz; $CDCl_3$; Me_4Si) 0.96 (3H, d, *J* = 6.6 Hz, 2-CH_3), 3.72–3.83 (2H, m, 2-H, 3-H), 4.89–4.97 (2H, m, 5-H), 5.94 (1H, ddd, *J* = 6.9, 13.6, 17.1 Hz, 4-H), 6.03 (1H, d, *J* = 8.2 Hz, 5′-H), 6.61–6.63 (2H, m, 7′-H), 7.22–7.35 (5H, m, Ar-H), 7.48 (1H, d, *J* = 1.6 Hz, 2′-H), 7.61 (1H, dd, *J* = 1.6, 8.2 Hz, 6′-H). **δ_C** (75 MHz; $CDCl_3$) 17.1 (2-CH_3), 44.7 (C-2), 52.8 (C-3), 101.8 (C-2′), 107.9 (C-7′), 108.1 (C-4′), 115.4 (C-5), 124.3 (C-6′), 126.6, 128.4, 128.6 (Ar-CH), 132.1 (C-5′), 139.8 (C-4), 141.7 (Ar-C), 148.3 (C-3a′), 151.7 (C-7a′), 201.6 (C-1). **IR:** ν_{max}(film)/cm^{-1}; 2977, 2860, 1622, 1241, 1110, 1033, 768, 735. The sample decomposed prior to mass spectrum acquisition.

4.2.3 General procedure: Wacker oxidation

To a solution of ketone (1 mmol) in DMF/H_2O (3:1, 100 mL) was added $PdCl_2$ (0.5 mmol) and CuCl (1.3 mmol) and the resultant suspension was stirred vigorously open to air. The mixture was filtered through a slurry of silica and ethyl acetate and was washed with ethyl actetate (3 × 100 mL). The solvent was removed *in vacuo*, the residue was diluted with ethyl acetate (30 mL) and water (30 mL) and the organic layer separated. The aqueous phase was further extracted with ethyl acetate (3 × 30 mL) and the combined organic extracts were washed with water (3 × 30 mL), dried ($MgSO_4$) and the solvent removed *in vacuo*. The crude product was purified by flash chromatography to yield the diketone product. All diketones **1** have 2,3-*syn* stereochemistry except those formed using ketones *anti*-**1a** and *anti*-**1b**.

4.2.3.1 (2R, 3R*)-1-(4′-Methoxyphenyl)-2,3-dimethylpentane-1,4-dione syn-****1a***. Using alkene **5a**. Flash chromatography using 2:1 hexanes, ethyl acetate to yield 0.39 g, 91% as a brown-green oil. **R_F** (2:1 hexanes, ethyl acetate) = 0.40. **δ_H** (400 MHz; $CDCl_3$; Me_4Si) 1.17 (6H, t, *J* = 7.1 Hz, 2-CH_3, 3-CH_3), 2.22 (3H, s, 5-CH_3), 3.07 (1H, pent., *J* = 7.2 Hz, 3-H), 3.69 (1H, pent., *J* = 7.2 Hz, 2-H), 3.87 (3H, s, OCH_3), 6.90–6.96 (2H, m, 3′-H), 7.91–7.97 (2H, m, 2′-H). **δ_C** (100 MHz; $CDCl_3$) 13.9 (2-CH_3), 15.3 (3-CH_3), 29.0 (C-5), 42.7 (C-2), 48.8 (C-3), 55.4 (OCH_3), 113.7 (C-3′), 128.9 (C-1′), 130.6 (C-2′), 163.3 (C-4′), 202.6 (C-4), 212.3 (C-1). **IR:** ν_{max}(film)/cm^{-1}; 2973, 1669, 1598, 1510, 1257, 1167, 1028. ***m/z*** (ESI^+) 257 (MNa^+, 100%). **HRMS** (ESI^+) found (MH^+): 235.1324; $C_{14}H_{19}O_3$ requires 235.1329.

4.2.3.2 (2S, 3R*)-1-(4′-Methoxyphenyl)-2,3-dimethylpentane-1,4-dione anti-****1a***. Using alkene *anti*-***5a***. Flash chromatography using 2:1 hexanes, ethyl acetate to yield 19 mg, 49% as a yellow oil. **R_F** (2:1 hexanes, ethyl acetate) = 0.47. **δ_H** (300 MHz; $CDCl_3$; Me_4Si) 2.04 (3H, d, *J* = 6.9 Hz, 3-CH_3), 1.13 (3H, d, *J* = 6.9 Hz, 2-CH_3), 2.24 (3H, s, 5-CH_3), 3.07 (1H, pent., *J* = 6.9 Hz, 3-H), 3.73 (1H, pent., *J* = 6.9 Hz, 2-H), 3.88 (3H, s, OCH_3), 6.95 (2H, d, *J* = 8.9 Hz, 3′-H), 7.98 (2H, d, *J* = 8.9 Hz, 2′-H). **δ_C** (75 MHz; $CDCl_3$) 16.0 (2-CH_3), 16.9 (3-CH_3), 30.4 (C-5), 42.3 (C-2), 49.4 (C-3), 55.5 (OCH_3), 113.9 (C-3′), 129.7 (C-1′), 130.7 (C-2′), 163.7 (C-4′), 201.7 (C-1), 212.1 (C-4). **IR:** ν_{max}(film)/cm^{-1}; 2972, 2935, 1710, 1669, 1599, 1259, 1169, 845. ***m/z*** (ESI^+) 257 (MNa^+, 100%). **HRMS** (ESI^+) found (MNa^+): 257.1150; $C_{14}H_{18}NaO_3$ requires 257.1148.

4.2.3.3 (2R, 3R*)-1-(Benzo[d][1′,3′]dioxol-5′-yl)-2,3-dimethylpentane-1,4-dione syn-****1b***. Using alkene **5b**. Flash chromatography using 19:1 hexanes, ethyl acetate to yield 0.40 g, 80% as a viscous colourless oil. **R_F** (2:1 hexanes, ethyl acetate) = 0.50. **δ_H** (400 MHz; $CDCl_3$; Me_4Si) 1.15–1.19 (6H, m, 2-CH_3, 3-CH_3), 2.21 (3H, s, 5-H), 3.03–3.11

(1H, m, 3-H), 3.60–3.67 (1H, m, 2-H), 6.03 (2H, s, 2′-H), 6.85 (1H, d, *J* = 8.2 Hz, 7′-H), 7.41 (1H, d, *J* = 1.6 Hz, 4′-H), 7.58 (1H, dd, *J* = 1.6, 8.2 Hz, 6′-H). **δ_C** (100 MHz; $CDCl_3$) 13.9 (2-CH_3), 15.4 (3-CH_3), 28.9 (C-5), 42.9 (C-2), 49.0 (C-3), 101.7 (C-2′), 107.9 (C-7′), 108.3 (C-4′), 124.5 (C-6′), 130.7 (C-5′), 148.1 (C-3a′), 151.6 (C-7a′), 202.2 (C-1), 212.2 (C-4). **IR:** ν_{max}(film)/cm^{-1}; 2975, 2917, 1705, 1659, 1601, 1498, 1444, 1250, 1101, 1035, 760, 738, 696. ***m/z*** (ESI^+) 271 (MNa^+, 100%), 227 (10). **HRMS** (ESI^+) found (MNa^+): 271.0944; $C_{14}H_{16}NaO_4$ requires 271.0941.

4.2.3.4 (2S, 3R*)-1-(Benzo[d][1′,3′]dioxol-5′-yl)-2,3-dimethylpentane-1,4-dione anti-**1b***. Using alkene *anti*-**5b**. Flash chromatography using 2:1 hexanes, ethyl acetate 78 mg, 68% as a yellow oil. **R_F** (2:1 hexanes, ethyl acetate) = 0.53. **δ_H** (400 MHz; $CDCl_3$; Me_4Si) 1.04 (3H, d, *J* = 6.8 Hz, 3-CH_3), 1.12 (3H, d, *J* = 6.8 Hz, 2-CH_3), 2.23 (3H, s, 5-H), 3.06 (1H, pent., *J* = 6.8 Hz, 3-H), 3.69 (1H, pent., *J* = 6.8 Hz, 2-H), 6.05 (2H, s, 2′-H), 6.87 (1H, d, *J* = 8.4 Hz, 7′-H), 7.46 (1H, d, *J* = 2.0 Hz, 4′-H), 7.61 (1H, dd, *J* = 2.0 Hz, 8.4 Hz, 6′-H). **δ_C** (100 MHz; $CDCl_3$) 15.8 (3-CH_3), 16.9 (2-CH_3), 30.2 (C-5), 42.4 (C-2), 49.3 (C-3), 101.8 (C-2′), 107.8 (C-4′), 108.0 (C-7′), 124.6 (C-6′), 131.5 (C-5′), 148.3 (C-3a′), 151.9 (C-7a′), 201.2 (C-1), 211.8 (C-4). **IR:** ν_{max}(film)/cm^{-1}; 2924, 2854, 1710, 1669, 1607, 1504, 1480, 1439, 1243, 1036, 808, 756. ***m/z*** (ESI^+) 271 (MNa^+, 100%). **HRMS** (ESI^+) found (MNa^+): 271.0945; $C_{14}H_{16}NaO_4$ requires 271.0954.

4.2.3.5 (2R, 3R*)-1-(3′,4′-Dimethoxyphenyl)-2,3-dimethylpentane-1,4-dione **1c***. Using alkene **5c**. Flash chromatography using 9:1 hexanes, ethyl acetate to yield 0.64 g, 98% as a pale yellow solid. **R_F** (2:1 hexanes, ethyl acetate) = 0.30. **MP:** 61–64 °C. **δ_H** (300 MHz; $CDCl_3$; Me_4Si) 1.18 (3H, d, *J* = 7.2 Hz, 2-CH_3), 1.20 (3H, d, *J* = 7.3 Hz, 3-CH_3), 2.22 (3H, s, 5-H), 3.09 (1H, pent., *J* = 7.3 Hz, 3-H), 3.70 (1H, pent., *J* = 7.2 Hz, 2-H), 3.93 (3H, s, 3′-OCH_3), 3.94 (3H, s, 4′-OCH_3), 6.90 (1H, d, *J* = 8.4 Hz, 5′-H), 7.50 (1H, d, *J* = 2.0 Hz, 2′-H), 7.63 (1H, dd, *J* = 2.0, 8.4 Hz, 6′-H). **δ_C** (75 MHz; $CDCl_3$) 13.9 (3-CH_3), 15.4 (2-CH_3), 28.9 (C-5), 42.6 (C-2), 48.9 (C-3), 55.8, 55.9 (3′-OCH_3, 4′-OCH_3), 110.0 (C-5′), 110.5 (C-2′), 122.8 (C-6′), 129.0 (C-1′), 149.0 (C-3′), 153.1 (C-4′), 202.6 (C-1), 212.2 (C-4). **IR:** ν_{max}(film)/cm^{-1}; 2970, 2936, 2841, 1710, 1667, 1594, 1584, 1514, 1456, 1258, 1158, 766, 754. ***m/z*** (ESI^+) 287 (MNa^+, 100%), 265 (20). **HRMS** (ESI^+) found (MNa^+): 287.1245; $C_{15}H_{20}NaO_4$ requires 287.1254.

4.2.3.6 (2R,3R*)-2,3-dimethyl-1-(3′,4′,5′-trimethoxyphenyl)pentane-1,4-dione **1d***. Using alkene **5d**. Flash chromatography using 2:1 hexanes, ethyl acetate to yield 0.16 g, 86% as a yellow oil. **R_F** = 0.29 (2:1 hexanes, ethyl acetate). **δ_H** (500 MHz; $CDCl_3$; Me_4Si) 1.18 (3H, d, *J* = 7.2 Hz, 2-CH_3), 1.22 (3H, d, *J* = 7.2 Hz, 3-CH_3), 2.23 (3H, s, 5-CH_3), 3.08–3.11 (1H, m, 3-H), 3.66–3.69 (1H, m, 2-H), 3.91 (3H, s, 4′-OCH_3), 3.92 (6H, s, 3′-OCH_3), 7.22 (2H, s, 2′-H). **δ_C** (125 MHz; $CDCl_3$) 14.0 (3-CH_3), 15.5 (2-CH_3), 29.1 (5-CH_3), 42.9 (C-2), 49.1 (C-3), 56.1 (3′-OCH_3, 4′-OCH_3), 105.9 (C-2′), 131.3 (C-1′), 142.5 (C-4′), 153.1 (C-3′), 203.1 (C-1), 212.3 (C-4). **IR**: (film)/cm-1; 2940, 2839, 1711, 1673, 1583, 1456, 1333, 1160, 1002, 908, 730. **m/z** (ESI+) 317 (MNa^+, 100%). **HRMS** (ESI+) Found (MNa^+): 317.1359; $C_{16}H_{22}NaO_5$ requires 317.1359.

4.2.3.7 (2S, 3R*)-1-(4′-Methoxyphenyl)-3-methyl-2-phenylpentane-1,4-dione **1e***. Using alkene **5e**. Flash chromatography using 9:1 hexanes, ethyl acetate to yield 24 mg, 72% as a yellow oil. **R_F** (2:1 hexanes, ethyl acetate) = 0.56. **δ_H** (400 MHz; $CDCl_3$; Me_4Si) 0.94 (3H, d, *J* = 7.2 Hz, 3-CH_3), 2.32 (3H, s, 5-H), 3.46 (1H, dq, *J* = 7.2, 10.8 Hz, 3-H), 3.78 (3H, s, OCH_3), 4.74 (1H, d, *J* = 10.8 Hz, 2-H), 6.81 (2H, d, *J* = 8.8 Hz, 3′-H), 7.27–7.29 (5H, m, Ar-H), 7.91 (2H, d, *J* = 8.8 Hz, 2′-H). **δ_C** (100 MHz; $CDCl_3$) 14.8 (3-CH_3), 29.2 (C-5), 49.9 (C-3), 55.3 (C-2), 56.5 (OCH_3), 113.6 (C-3′), 127.3, 128.7, 129.0 (Ar-CH), 129.3 (C-1′), 131.1 (C-2′), 137.5 (C-1″), 163.2 (C-4′), 198.2 (C-1), 212.5 (C-4). **IR:** ν_{max}(film)/cm^{-1}; 2968, 2935, 2841, 1710, 1667, 1597, 1575, 1510, 1454, 1260, 1233, 1029, 743, 702. ***m/z*** (ESI^+) 319 (MNa^+, 100%). **HRMS** (ESI^+) found (MNa^+): 319.1298; $C_{19}H_{20}NaO_3$ requires 319.1305.

4.2.3.8 (3R, 4S*)-3-Methyl-4-phenylnonane-2,5-dione **1f***. Using alkene **5f**. Flash chromatography using 2:1 hexanes, ethyl acetate to yield 50 mg, quant. as a yellow oil. **R_F** (2:1 hexanes, ethyl acetate) = 0.81. **δ_H** (300 MHz; $CDCl_3$; Me_4Si) 0.75–0.85 (6H, m, 3-CH_3, 9-H), 1.11–1.17 (2H, m, 8-H), 1.39–1.52 (2H, m, 7-H), 2.28 (3H, s, 1-H), 2.31–2.41 (2H, m, 6-H), 3.28–3.35 (1H, m, 3-H), 3.95 (1H, d, *J* = 12.0 Hz, 4-H), 7.15–7.33 (5H, m, Ar-H). **δ_C** (75 MHz; $CDCl_3$) 13.7 (3-CH_3), 14.6 (C-9), 22.0 (C-8), 25.6 (C-7), 29.0 (C-1), 41.3 (C-6), 48.6 (C-3), 61.4 (C-4), 127.5, 128.8, 129.0 (Ar-CH), 136.5 (Ar-C), 210.4 (C-5), 212.4 (C-2). **IR:** ν_{max}(neat)/cm^{-1}; 2959, 2933, 2874, 1707, 1494, 1454, 742. ***m/z*** (ESI^+) 269 (MNa^+, 100%), 247 (60), 229 (20), 175 (40). **HRMS** (ESI^+) found (MH^+): 247.1691; $C_{16}H_{23}O_2$ requires 247.1693.

4.2.3.9 (2R, 3R*)-1-(4′-Methoxyphenyl)-3-methyl-2-propylpentane-1,4-dione **1g***. Using alkene **5g**. Flash chromatography using 2:1 hexanes, ethyl acetate to yield 58 mg, 55% as a colourless oil. **R_F** (2:1 hexanes, ethyl acetate) = 0.57. **δ_H** (300 MHz; $CDCl_3$; Me_4Si) 0.81 (3H, t, *J* = 7.2 Hz, 2-$CH_2CH_2CH_3$), 1.08–1.26 (2H, m, 2-$CH_2CH_2CH_3$), 1.17 (3H, d, *J* = 7.3 Hz, 3-CH_3), 1.50–1.73 (2H, m, 2-$CH_2CH_2CH_3$), 2.18 (3H, s, 5-H), 3.07–3.17 (1H, m, 2-H), 3.72 (1H, dq, *J* = 4.0, 8.1 Hz, 3-H), 3.86 (3H, s, OCH_3), 6.93 (2H, d, *J* = 8.8 Hz, 3′-H), 7.95 (2H, d, *J* = 8.8 Hz, 2′-H). **δ_C** (75 MHz; $CDCl_3$) 13.9 (3-CH_3), 14.4 (2-$CH_2CH_2CH_3$), 19.7 (2-$CH_2CH_2CH_3$), 29.1 (C-5), 31.6 (2-$CH_2CH_2CH_3$), 47.3 (C-2), 47.6 (C-3), 55.4 (OCH_3), 113.7 (C-3′), 130.6 (C-2′, C-1′), 163.4 (C-4′), 202.7 (C-1), 212.0 (C-4). **IR:** ν_{max}(film)/cm^{-1}; 2959, 2935, 2874, 1711, 1668, 1598, 1574, 1509, 1461, 1167, 842, 771. ***m/z*** (ESI^+) 285 (MNa^+, 100%), 263 (40), 155 (40). **HRMS** (ESI^+) found (MH^+): 263.1640; $C_{16}H_{23}O_3$ requires 263.1642.

4.2.3.10 (2R, 3R*)-1-(Benzo[d][1″,3″]dioxol-5″-yl)-2-(benzo[d][1′,3′]dioxol-5′-ylmethyl)-3-methylpentane-1,4-dione **1h***. Using alkene **5h**. Flash chromatography using 9:1 hexanes, ethyl acetate to yield 84 mg, 69% as a yellow oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.47. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 1.23 (3H, d, *J* = 7.4 Hz, 3-CH_3), 2.17 (3H, s, 5-H), 2.81–2.90 (2H, m, 2-CH_2), 3.03 (1H, pent., *J* = 7.4 Hz, 3-H), 3.88–3.93 (1H, m, 2-H), 5.84 (2H, s, 2″-H), 5.98 (2H, s, 2′-H), 6.48 (1H, dd, *J* = 1.2, 8.0 Hz, 6′-H), 6.53 (1H, d, *J* = 1.2 Hz, 4′-H), 6.59 (1H, *J* = 8.0 Hz, 7′-H), 6.74 (1H, d, *J* = 8.4 Hz, 7″-H), 7.27 (1H, d, *J* = 1.6 Hz, 4″-H), 7.36 (1H, dd, *J* = 1.6, 8.4 Hz, 6″-H). $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 13.8 (3-CH_3), 29.0 (C-5), 35.0 (2-CH_2), 48.0 (C-3), 49.8 (C-2), 100.7 (C-2′), 101.7 (C-2″), 107.7 (C-7′), 108.0 and 108.1 (C-4′ and C-7″), 109.4 (C-4″), 122.0 (C-6″), 124.5 (C-6′), 131.9 (C-5′), 132.2 (C-5″), 145.9 (C-7a′), 147.3 (C-3a′), 147.9 (C-3a″), 151.5 (C-7a″), 201.3 (C-1), 211.3 (C-4). **IR:** ν_{max}(film)/cm^{-1}; 2900, 1708, 1666, 1502, 1487, 1439, 1243, 1034, 928, 808, 731. ***m/z*** (ESI^+) 391 (MNa^+, 100%), 227 (40). **HRMS** (ESI^+) found (MNa^+): 391.1144; $C_{21}H_{20}NaO_6$ requires 391.1152.

4.2.3.11 (2R, 3R*)-2-(Benzo[d][1′,3′]dioxol-5′-ylmethyl)-1-(4″-methoxyphenyl)-3-methylpentane-1,4-dione **1i***. Using alkene **5i**. Flash chromatography using 9:1 hexanes, ethyl acetate to yield 0.14 g, 83% as a yellow oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.59. $\boldsymbol{\delta_H}$ (300 MHz; $CDCl_3$; Me_4Si) 1.22 (3H, d, *J* = 7.2 Hz, 3-CH_3), 2.16 (3H, s, 5-H), 2.79–2.94 (2H, m, 2-CH_2), 3.03 (1H, pent., *J* = 7.2 Hz, 3-H), 3.79 (3H, s, OCH_3), 3.97 (1H, pent., *J* = 4.2 Hz, 2-H), 5.80 (2H, s, 2′-H), 6.48–6.64 (3H, m, 4′-H, 6′-H, 7′-H), 6.82 (2H, d, *J* = 8.6 Hz, 3″-H), 7.78 (2H, d, *J* = 8.6 Hz, 2″-H). $\boldsymbol{\delta_C}$ (75 MHz; $CDCl_3$) 13.6 (3-CH_3), 28.8 (C-5), 34.7 (2-CH_2), 47.8 (C-2), 49.5 (C-3), 55.2 (OCH_3), 100.5 (C-2′), 107.8 (C-7′), 109.3 (C-4′), 113.4 (C-3″), 121.9 (C-6′), 129.9 (C-1″), 130.4 (C-2″), 132.3 (C-5′), 145.7, 147.2 (C-7a′, C-3a′), 163.1 (C-4″), 201.4 (C-1), 211.2 (C-4). **IR:** ν_{max}(film)/cm^{-1}; 2975, 2935, 2896, 2842, 1708, 1667, 1598, 1504, 1488, 1442, 906, 724. ***m/z*** (ESI^+) 377 (MNa^+, 100%), 355 (20), 337 (15). **HRMS** (ESI^+) found (MNa^+): 377.1355; $C_{21}H_{22}NaO_5$ requires 377.1359.

*4.2.3.12 1-(3′-isopropoxy-4′-methoxyphenyl)-3-methylpentane-1,4-dione **1j***. Using alkene **5j**. Flash chromatography using 19:1 n-hexanes, ethyl acetate to yield 0.22 g, 76% as a yellow oil. $\mathbf{R_F}$ = 0.40 (2:1 hexanes, ethyl acetate). $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 1.17 (3H, d, *J* = 7.2 Hz, 3-CH_3), 1.35 (6H, d, *J* = 6.0 Hz, 3′-OCH(CH_3)$_2$), 2.28 (3H, s, 5-CH_3), 2.86–2.91 (1H, m, 2-CH_2), 3.17–3.21 (1H, m, 3-H), 3.42–3.48 (1H, m, 2-CH_2), 3.89 (3H, s, 4′-OCH_3), 4.57–4.60 (1H, m, 3′-OC*H*(CH_3)$_2$), 6.85 (1H, d, *J* = 8.4 Hz, 5′-H) , 7.49 (1H, d, *J* = 2.0 Hz, 2′-H), 7.56 (1H, dd, *J* = 8.4, 2.0 Hz, 6′-H). $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 16.7 (3-CH_3), 21.9 (3′-OCH(CH_3)$_2$), 28.8 (5-CH_3), 41.5 (C-2), 41.8 (C-3), 56.0 (4′-OCH_3), 71.4 (3′-O*C*H(CH_3)$_2$), 110.6 (C-5′), 114.2 (C-2′), 123.0 (C-6′), 130.2 (C-1′), 147.2 (C-3′), 154.7 (C-4′), 197.9 (C-1), 211.7 (C-4). **IR**: (film)/cm-1; 3079, 2934, 2841, 1714, 1672, 1592, 1425, 1269, 1162, 1021, 961, 775. **m/z** (ESI+) 301 (MNa^+, 100%). **HRMS** (ESI+) Found (MNa^+): 301.1420; $C_{16}H_{22}NaO_4$ requires 301.1410.

*4.2.3.13 1-(4′-Methoxyphenyl)-2-methylpentane-1,4-dione **1k***. Using alkene **5k**. Flash chromatography using 9:1 hexanes, ethyl acetate to yield 46 mg, 77% as a yellow oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.48. $\boldsymbol{\delta_H}$ (300 MHz; $CDCl_3$; Me_4Si) 1.15 (3H, d, *J* = 7.2 Hz, 2-CH_3), 2.14 (3H, s, 5-H), 2.47–2.54 (1H, m, 3-H_A), 3.07–3.16 (1H, m, 3-H_B), 3.84 (3H, s, OCH_3), 3.86–3.94 (1H, m, 2-H), 6.92 (2H, d, *J* = 8.8 Hz, 3′-H), 7.95 (2H, d, *J* = 8.8 Hz, 2′-H). Spectroscopic data were in accordance with literature values.[26]

*4.2.3.14 1-(4′-Methoxyphenyl)-2-phenylpentane-1,4-dione **1m***. Using alkene **5m**. Flash chromatography using 9:1 hexanes, ethyl acetate to yield 74 mg, 54% as a colourless oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.68. $\boldsymbol{\delta_H}$ (300 MHz; $CDCl_3$; Me_4Si) 2.16 (3H, s, 5-H), 2.68 (1H, dd, *J* = 3.9, 17.7 Hz, 3-H_A), 3.57 (1H, dd, *J* = 9.9, 17.7 Hz, 3-H_B), 3.76 (3H, s, OCH_3), 5.06 (1H, dd, *J* = 3.9, 9.9 Hz, 2-H), 6.82 (2H, d, *J* = 9.0 Hz, 3′-H), 7.16–7.29 (5H, m, Ar-H), 7.93 (2H, d, *J* = 9.0 Hz, 2′-H). Spectroscopic data were in accordance with literature values.[26]

4.2.3.15 (2R, 3S*)-1-(Benzo[d][1′,3′]dioxol-5′-yl)-2-methyl-3-phenylpentane-1,4-dione **1n***. Using alkene **5n**. Flash chromatography using 9:1 hexanes, ethyl acetate to yield 66 mg, 96% as a pale yellow oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.69. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 0.91 (3H, d, *J* = 7.6 Hz, 2-CH_3), 2.07 (3H, s, 5-H), 4.02 (1H, dq, *J* = 7.6, 10.8 Hz, 2-H), 4.23 (1H, d, *J* = 10.8 Hz, 3-H), 6.03 (2H, s, 2′-H), 6.87 (1H, d, *J* = 8.3 Hz, 7′-H), 7.27–7.39 (5H, m, Ar-H), 7.48 (1H, d, *J* = 1.6 Hz, 4′-H), 7.66 (1H, dd, *J* = 1.6, 8.3 Hz, 6′-H). $\boldsymbol{\delta_C}$ (75 MHz; $CDCl_3$) 16.3 (2-CH_3), 29.2 (C-5), 43.4 (C-2), 62.3 (C-3), 101.7 (C-2′), 107.9 (C-7′), 108.3 (C-4′), 124.6 (C-6′), 127.7, 128.9, 129.0 (Ar-CH), 130.7 (C-5′), 136.5 (Ar-C), 148.1 (C-3a′), 151.7 (C-7a′), 202.1 (C-1), 207.9 (C-4). **IR:** ν_{max}(film)/cm^{-1}; 2975, 2911, 1705, 1659, 1602, 1499, 1444, 1250, 1101, 1035, 932, 760, 696. ***m/z*** (ESI^+) 333 (MNa^+, 100%). **HRMS** (ESI^+) found (MNa^+): 333.1102; $C_{19}H_{18}NaO_4$ requires 333.1097.

4.2.4 General procedure: Synthesis of pyrroles

To a solution of diketone (1 mmol) and NaOAc (1.1 mmol) in acetic acid (15 mL) was added dropwise amine (1.1 mmol) dropwise and the resultant mixture was stirred vigorously at 80 °C, open to air, for the time stated. Alternatively the reaction was stirred under an atmosphere of nitrogen if specifically stated.The mixture was cooled to room temperature and neutralized to pH 7 using NaOH solution. Ethyl acetate (15 mL) was added, the organic layer separated and the aqueous phase further extracted with ethyl acetate (3 × 15 mL). The combined organic extracts were

dried ($MgSO_4$) and the solvent removed *in vacuo*. The crude product was then purified by flash chromatography to yield the pyrrole product.

4.2.4.1 5-(4′-Methoxyphenyl)-3,4-dimethyl-1-(3″-phenylpropyl)-1H-pyrrole-2-carbaldehyde ***8a***. Using diketone **1a**. Flash chromatography using 2:1 hexanes, ethyl acetate to yield 86 mg, 58% as a viscous green-brown oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.65. $\boldsymbol{\delta_H}$ (300 MHz; $CDCl_3$; Me_4Si) 1.22–1.34 (2H, m, 2″-H), 1.85 (3H, s, 3-CH_3), 2.30 (3H, s, 4-CH_3), 2.46 (2H, t, *J* = 7.8 Hz, 3″-H), 3.87 (3H, s, OCH_3), 4.20 (2H, t, *J* = 7.8 Hz, 1″-H), 6.87–7.00 (3H, m, 3′-H, Ar-H), 7.10–7.21 (4H, m, Ar-H), 7.96 (2H, dd, *J* = 1.9, 8.9 Hz, 2′-H), 9.72 (1H. s, CHO). $\boldsymbol{\delta_C}$ (75 MHz; $CDCl_3$) 9.1, 9.2 (3-CH_3, 4-CH_3), 29.7 (C-2″), 32.7 (C-3″), 45.3 (C-1″), 55.3 (OCH_3), 113.5 (C-3′), 122.1 (C-1′), 123.0 (C-4), 125.7 (C-2, C-3), 128.1, 128.2 (Ar-CH), 130.7 (C-2′), 131.7 (Ar-CH), 141.3 (Ar-C), 159.7 (C-4′, C-5), 177.1 (CHO). **IR:** ν_{max}(film)/cm^{-1}; 2921, 2954, 2854, 1672, 1601, 1510, 1259, 1171, 1030. ***m/z*** (ESI^+) 370 (MNa^+, 100%), 348 (60). **HRMS** (ESI^+) found (MH^+): 348.1970; $C_{23}H_{26}NO_2$ requires 348.1958.

4.2.4.2 5-(Benzo[d][1′,3′]dioxol-5′-yl)-1-benzyl-3,4-dimethyl-1H-pyrrole-2-carbaldehyde ***8b***. Using diketone **1b**. Flash chromatography using 3:1 hexanes, ethyl acetate to yield 17 mg, 52% as a yellow oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.55. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 1.92 (3H, s, 3-CH_3), 2.33 (3H, s, 4-CH_3), 5.45 (2H, s, 1-CH_2), 5.99 (2H, s, 2′-H), 6.64–6.66 (2H, m, 6′-H, 7′-H), 6.80–6.85 (3H, m, 4′-H, Ar-H), 7.16–7.23 (3H, m, Ar-H), 9.70 (1H, s, CHO). $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 9.3 (4-CH_3), 9.4 (3-CH_3), 48.8 (1-CH_2), 101.3 (C-2′), 108.4 (C-4′), 110.4 (C-7′), 118.8 (C-3), 124.1 (C-5′), 124.2 (C-6′), 126.1, 126.9 (Ar-CH), 127.2 (C-5), 128.3 (Ar-CH), 133.7 (C-4), 139.0 (C-2), 141.0 (Ar-C), 147.7, 147.9 (C-7a′, C-3a′), 177.5 (CHO). **IR:** ν_{max}(film)/cm^{-1}; 2911, 1647, 1467, 1242, 1223, 1037, 822, 730. ***m/z*** (ESI^+) 356 (MNa+, 100%). **HRMS** (ESI^+) found (MNa^+): 356.1254; $C_{21}H_{19}NNaO_3$ requires 356.1257.

4.2.4.3 4″-(2-(4′-Methoxyphenyl)-3,4,5-trimethyl-1H-pyrrol-1-yl)benzenesulfonamide ***8c***. Using diketone **1a**. Flash chromatography using 4:1 hexanes, ethyl acetate to yield 51 mg, 65% as a yellow oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.22. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 2.04, 2.06, 2.08 (9H, s, 3-OCH_3, 4-OCH_3, 5-CH_3), 3.72 (3H, s, OCH_3), 5.18 (2H, s, NH_2), 6.72 (2H, d, *J* = 8.8 Hz, 3′-H), 6.91 (2H, d, *J* = 8.8 Hz, 2′-H), 7.12 (2H, d, *J* = 8.8 Hz, 2″-H), 7.78 (2H, d, *J* = 8.8 Hz, 3″-H). $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 9.5 (4-CH_3), 10.0 (3-CH_3), 11.1 (5-CH_3), 55.0 (OCH_3), 113.5 (C-3′), 116.4 (C-4), 117.5 (C-3), 125.0 (C-1′), 125.3 (C-5), 126.9 (C-3″), 128.7 (C-2″), 129.2 (C-2), 131.3 (C-2′), 139.4 (C-1″), 143.6 (C-4″), 157.8 (C-4′). **IR:** ν_{max}(film)/cm^{-1}; 3296, 2961, 2925, 1597, 1500, 1457, 1250, 1027, 1162, 828. The sample decomposed prior to mass spectrum acquisition.

4.2.4.4 1-Benzyl-5-(4′-methoxyphenyl)-3,4-dimethyl-1H-pyrrole-2-carbaldehyde ***8d***. Using diketone **1a**. Flash chromatography using 9:1 hexanes, ethyl acetate to yield 25 mg, 26% as a yellow oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.59. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 1.91 (3H, s, 3-CH_3), 2.33 (3H, s, 4-CH_3), 3.81 (3H, s, OCH_3), 5.44 (2H, s, 1-CH_2), 6.83–6.86 (2H, m, Ar-H), 6.90 (2H, d, *J* = 8.8 Hz, 3′-H), 7.10 (2H, d, *J* = 8.8 Hz, 2′-H), 7.14–7.25 (3H, m, Ar-H), 9.71 (1H, s, CHO). $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 9.3 (4-CH_3), 9.4 (3-CH_3), 48.8 (1-CH_2), 55.2 (OCH_3), 113.9 (C-3′), 118.8 (C-4), 122.8 (C-1′), 126.1, 126.8 (Ar-CH), 127.2 (C-2), 128.3 (Ar-CH), 131.4 (C-2′), 133.8 (C-3), 139.1 (Ar-C), 141.4 (C-5), 159.8 (C-4′), 177.4 (CHO). **IR:** ν_{max}(film)/cm^{-1}; 2934, 2837, 1642, 1610, 1455, 1246, 1028, 1176, 842, 789, 730, 697. ***m/z*** (ESI^+) 342 (MNa^+, 100%), 330 (50), 320 (20), 271 (10). **HRMS** (ESI^+) found (MNa^+): 342.1464; $C_{21}H_{21}NNaO_2$ requires 342.1465.

4.2.4.5 1-Butyl-5-(4′-methoxyphenyl)-3,4-dimethyl-1H-pyrrole-2-carbaldehyde ***8e***. Using diketone **1a**. Flash chromatography using 2:1 hexanes, ethyl acetate to yield 41 mg, 34% as a yellow oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.65. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 0.75 (3H, t, *J* = 8.0 Hz, 1-$CH_2CH_2CH_2CH_3$), 1.06–1.15 (2H, m, 1-$CH_2CH_2CH_2CH_3$), 1.48–1.54 (2H, m, 1-$CH_2CH_2CH_2CH_3$), 1.86 (3H, s, 4-CH_3), 2.31 (3H, s, 3-CH_3), 3.87 (3H, s, OCH_3), 4.13 (2H, t, *J* = 8.0 Hz, 1-$CH_2CH_2CH_2CH_3$), 6.99 (2H, d, *J* = 8.8 Hz, 3′-H), 7.20 (2H, d, *J* = 8.8 Hz, 2′-H), 9.73 (1H, s, CHO). $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 9.2, 9.3 (3-CH_3, 4-CH_3), 13.6 (1-$CH_2CH_2CH_2CH_3$), 19.7 (1-$CH_2CH_2CH_2CH_3$), 33.7 (1-$CH_2CH_2CH_2CH_3$), 45.5 (1-$CH_2CH_2CH_2CH_3$), 55.3 (OCH_3), 114.0 (C-2′), 118.3 (C-1′), 131.4 (C-3′, C-4), 133.4 (C-2, C-3), 141.0 (C-5), 159.6 (C-4′), 177.1 (CHO). **IR:** ν_{max}(film)/cm^{-1}; 2957, 2925, 2861, 1639, 1613, 1511, 1246, 1176, 1028. ***m/z*** (ESI^+) 286 (MH^+, 90%), 274 (10), 257 (3), 227 (3), 217 (8). **HRMS** (ESI^+) found (MH^+): 286.1803; $C_{18}H_{24}NO_2$ requires 286.1802.

4.2.4.6 2-(4′-Methoxyphenyl)-3,4,5-trimethyl-1-phenyl-1H-pyrrole ***8f***. Using diketone **1a**. Flash chromatography using 2:1 hexanes, ethyl acetate to yield 89 mg, 72% as a yellow oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.32. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 2.08 (9H, s, 3-CH_3, 4-CH_3, 5-CH_3), 3.73 (3H, s, OCH_3), 6.70 (2H, d, *J* = 8.7 Hz, 3′-H), 6.95 (2H, d, *J* = 8.7 Hz, 2′-H), 7.02–7.06 (2H, m, Ar-H), 7.22–7.26 (3H, m, Ar-H). $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 9.5, 10.1, 10.9 (3-CH_3, 4-CH_3, 5-CH_3), 55.0 (OCH_3), 113.2 (C-3′), 113.5 (C-4), 116.1 (C-1′), 125.5 (C-3), 125.7 (C-5), 126.5, 128.5, 128.6 (Ar-CH), 130.7 (C-2), 131.3 (C-2′), 139.7 (Ar-C), 157.6 (C-4′). **IR:** ν_{max}(film)/cm^{-1}; 2914, 1595, 1497, 1244, 1176, 1030. ***m/z*** (ESI^+) 292 (MH^+, 100%), 290 (60). **HRMS** (ESI^+) found (MH^+): 292.1707; $C_{20}H_{22}NO$ requires 292.1696.

4.2.4.7 5-(Benzo[d][1′,3′]dioxol-5′-yl)-1-(2″,6″-dimethoxyphenyl)-3,4-dimethyl-1H-pyrrole-2-carbaldehyde ***8g***. Using diketone **1b**. Flash chromatography using 2:1 hexanes, ethyl acetate to yield 15 mg, 30% b.r.s.m. as a yellow-green

oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.31. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 2.03 (3H, s, 4-CH_3), 2.43 (3H, s, 3-CH_3), 3.65 (6H, s, 2″-OCH_3), 5.92 (2H, s, 2′-H), 6.55 (1H, t, *J* = 1.5 Hz, 4′-H), 6.60 (1H, d, *J* = 7.6 Hz, 7′-H), 6.68 (1H, dd, *J* = 1.5, 7.6 Hz, 6′-H), 6.83 (3H, d, *J* = 1.6 Hz, 3″-H, 4″-H), 9.41 (1H, s, CHO). $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 9.5 (4-CH_3), 10.3 (3-CH_3), 55.7, 56.1 (2″-OCH_3), 101.1 (C-2′), 107.9 (C-7′), 110.0 (C-4′), 114.8 (C-3″), 116.1 (C-4″), 119.4 (C-3), 123.9 (C-6′), 124.7 (C-5′), 126.8 (C-1″), 129.0 (C-5), 130.9 (C-4), 138.8 (C-2), 147.2 (C-2″), 150.0, 153.1 (C-7a′, C-3a′), 179.5 (CHO). **IR:** ν_{max}(film)/cm^{-1}; 2921, 1651, 1507, 1463, 1242, 1225, 1036, 809, 729. ***m/z*** (ESI^+) 402 (MNa^+, 100%), 360 (90). **HRMS** (ESI^+) found (MNa^+): 402.1302; $C_{22}H_{21}NNaO_5$ requires 402.1312.

4.2.4.8 2-(3′,4′-Dimethoxyphenyl)-3,4,5-trimethyl-1-phenyl-1H-pyrrole ***8h***. Using diketone **1c**. Flash chromatography using 14:1 hexanes, ethyl acetate to yield 15 mg, 25% as a yellow oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.63. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 2.06 (6H, s, 2-CH_3, 3-CH_3), 2.12 (3H, s, 4-CH_3), 3.53 (3H, s, 4′-OCH_3), 3.83 (3H, s, 3′-OCH_3), 6.42 (1H, s, 5′-H), 6.69–6.75 (2H, m, 2′-H, 6′-H), 7.05–7.08 (1H, m, Ar-H), 7.22–7.30 (4H, m, Ar-H). $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 9.5 (3-CH_3), 10.2 (4-CH_3), 10.9 (5-CH_3), 55.4 (3′-OCH_3), 55.7 (4′-OCH_3), 110.5 (C-2′), 113.6 (C-5′), 122.5 (C-6′), 115.2 (C-4), 116.2 (C-3), 125.7 (C-1′), 125.9 (C-5), 126.6, 128.5, 128.6 (Ar-CH), 129.4 (C-2), 139.7 (Ar-C), 147.0 (C-4′), 148.0 (C-3′). **IR:** ν_{max}(film)/cm^{-1}; 2926, 2855, 1597, 1501, 1251, 1139, 1026, 763, 699. ***m/z*** (ESI^+) 344 (MNa^+, 10%), 360 (100). **HRMS** (ESI^+) found (MNa^+): 344.1603; $C_{21}H_{23}NNaO_2$ requires 344.1621.

4.2.4.9 4″-(2-(3′,4′-Dimethoxyphenyl)-3,4,5-trimethyl-1H-pyrrol-1-yl)benzenesulfonamide ***8i***. Using diketone **1c**. Flash chromatography using 19:1 hexanes, ethyl acetate to yield 34 mg, 74% b.r.s.m. as a pink oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.14. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 2.07, 2.08, 2.10 (9H, s, 3-CH_3, 4-CH_3, 5-CH_3), 3.59 (3H, s, 3′-OCH_3), 3.82 (3H, s, 4′-OCH_3), 4.95 (2H, s, NH_2), 6.44 (1H, d, *J* = 2.0 Hz, 2′-H), 6.62 (1H, dd, *J* = 2.0, 8.2 Hz, 6′-H), 6.73 (1H, d, *J* = 8.2 Hz, 5′-H), 7.17 (2H, d, *J* = 8.6 Hz, 2″-H), 7.81 (2H, d, *J* = 8.6 Hz, 3″-H). $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 9.5 (4-CH_3), 10.1 (3-CH_3), 11.1 (5-CH_3), 55.6, 55.7 (3′-OCH_3, 4′-OCH_3), 110.8 (C-2′), 113.5 (C-5′), 116.6 (C-4), 117.6 (C-3), 122.7 (C-6′), 125.3 and 125.4 (C-5, C-1′), 127.0 (C-3″), 128.7 (C-2″), 129.4 (C-2), 139.6 (C-1″), 143.7 (C-4″), 147.4 (C-4′), 148.2 (C-3′). **IR:** ν_{max}(film)/cm^{-1}; 3256, 2952, 2930, 2862, 1595, 1505, 1252, 1139, 1022, 1162, 836, 732. ***m/z*** (ESI^+) 423 (MNa^+, 100%), 400 (20). **HRMS** (ESI^+) found (MNa^+): 423.1355; $C_{21}H_{24}N_2NaO_4S$ requires 423.1349.

4.2.4.10 1-Benzyl-5-(3′,4′-dimethoxyphenyl)-3,4-dimethyl-1H-pyrrole-2-carbaldehyde ***8j***. Using diketone **1c**. Flash chromatography using 4:1 hexanes, ethyl acetate to yield 24 mg, 48% as a yellow oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.65. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 1.94 (3H, s, 3-CH_3), 2.36 (3H, s, 4-CH_3), 3.55 (3H, s, 4′-OCH_3), 3.90 (3H, s, 3′-OCH_3), 5.44 (2H, s, 1-CH_2), 6.54 (1H, d, *J* = 2.0 Hz, 2′-H), 6.78 (1H, dd, *J* = 2.0, 8.0 Hz, 6′-H), 6.88 (1H, d, *J* = 8.0 Hz, 5′-H), 7.16–7.27 (5H, m, Ar-H), 9.73 (1H, s, CHO). $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 9.3 (4-CH_3), 9.4 (3-CH_3), 49.1 (1-CH_2), 55.5 (4′-OCH_3), 55.8 (3′-OCH_3), 110.9 (C-5′), 113.0 (C-2′), 118.8 (C-3), 122.8 (C-6′), 126.0, 128.2 (Ar-CH), 126.8 (C-1′), 127.2 (C-2), 128.4 (Ar-CH), 133.8 (C-4), 139.3 (Ar-C), 141.5 (C-5), 148.5 (C-4′), 149.2 (C-3′), 177.4 (CHO). **IR:** ν_{max}(film)/cm^{-1}; 2934, 2836, 1644, 1436, 1247, 1139, 814, 731, 698. ***m/z*** (ESI^+) 372 (MNa^+, 100%), 350 (80). **HRMS** (ESI^+) found (MNa^+): 372.1536; $C_{22}H_{23}NNaO_3$ requires 372.1570.

4.2.4.11 (S)-5-(3′,4′-Dimethoxyphenyl)-3,4-dimethyl-1-(1-phenylethyl)-1H-pyrrole-2-carbaldehyde ***8k***. Using diketone **1c**. Flash chromatography using 2:1 hexanes, ethyl acetate to yield 13 mg, 26% as a pink oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.65. $\boldsymbol{\alpha_D}$ = +86 (*c* = 1.3, $CHCl_3$). $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 1.76 (3H, d, *J* = 6.8 Hz, 1-CHC*H*$_3$), 1.87 (3H, s, 3-CH_3), 2.36 (3H, s, 4-CH_3), 3.63 (3H, s, 4′-OCH_3), 3.89–3.97 (4H, m, 3′-OCH_3, 1-C*H*CH_3), 6.85 (1H, d, *J* = 8.2 Hz, 5′-H), 6.99–7.07 (2H, m, 2′-H, 6′-H), 7.14–7.34 (5H, m, Ar-H), 9.63 (1H, s, CHO). $\boldsymbol{\delta_C}$ (75 MHz; $CDCl_3$) 9.3 (4-CH_3), 9.9 (3-CH_3), 19.1 (1-CH(CH_3)Ar), 54.4 (1-*C*HCH_3), 55.0, 55.9 (3′-OCH_3, 4′-OCH_3), 110.9 (C-5′), 113.2 (C-2′), 119.1 (C-3), 122.9 (C-6′), 124.1 (C-1′), 125.8, 126.7 (Ar-CH), 127.2 (C-4), 128.2 (Ar-CH), 133.6 (C-2), 141.1 (C-5), 142.5 (Ar-C), 148.6 (C-4′), 149.2 (C-3′), 177.8 (CHO). **IR:** ν_{max}(film)/cm^{-1}; 2936, 2839, 1642, 1465, 1258, 1244, 1026, 1139, 766, 744, 698. ***m/z*** (ESI^+) 386 (MNa^+, 100%), 253 (20). **HRMS** (ESI^+) found (MNa^+): 386.1726; $C_{23}H_{25}NNaO_3$ requires 386.1727.

4.2.4.12 5-(3′,4′-Dimethoxyphenyl)-3,4-dimethyl-1-(3″-phenylpropyl)-1H-pyrrole-2-carbaldehyde ***8m***. Using diketone **1c**. Flash chromatography using 2:1 hexanes, ethyl acetate to yield 13 mg, 25% as a brown oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.80. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 1.85–1.89 (5H, m, 3-CH_3, 2″-H), 2.31 (3H, s, 4-CH_3), 2.46 (2H, t, *J* = 8.0 Hz, 3″-H), 3.83 (3H, s, 4′-OCH_3), 3.95 (3H, s, 3′-OCH_3), 4.20 (2H, t, *J* = 8.0 Hz, 1″-H), 6.70 (1H, d, *J* = 1.6 Hz, 2′-H), 6.79 (1H, dd, *J* = 1.6, 8.0 Hz, 6′-H), 6.90 (1H, d, *J* = 8.4 Hz, 5′-H), 6.98–7.00 (2H, m, Ar-H), 7.11–7.19 (3H, m, Ar-H), 9.73 (1H, s, CHO). $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 9.1 (4-CH_3), 9.3 (3-CH_3), 32.8 (C-2″, C-3″), 45.4 (C-1″), 55.9 (3′-OCH_3, 4′-OCH_3), 111.1 (C-5′), 113.0 (C-2′), 118.3 (C-3), 122.8 (C-6′), 123.3 (C-1′), 125.7 (Ar-CH), 126.9 (C-2), 128.1, 128.2 (Ar-CH), 133.6 (C-4), 141.0 (C-5), 141.2 (Ar-C), 148.8 (C-4′), 149.2 (C-3′), 177.2 (CHO). **IR**: ν_{max}(film)/cm^{-1}; 2931, 2856, 1641, 1260, 1245, 1139, 1027, 751, 700. ***m/z*** (ESI^+) 388 (100), 400 (MNa^+, 80%). **HRMS** (ESI^+) found (MNa^+): 400.1878; $C_{24}H_{27}NNaO_3$ requires 400.1883.

4.2.4.13 1-(3″-((tert-butyldiphenylsilyl)oxy)-4″-methoxyphenyl)-3,4,5-trimethyl-2-(3′,4′,5′-trimethoxyphenyl)-1H-pyrrole ***8n***. Using diketone **1d**. Flash chromatography using 19:1 hexanes, ethyl acetate 0.16 g, 74% as a pale yellow

oil. $\mathbf{R_F}$ = 0.77 (2:1 hexanes, ethyl acetate). $\boldsymbol{\delta_H}$ (500 MHz; $CDCl_3$; Me_4Si) 1.03 (9H, s, SiC(CH_3)$_3$), 1.72 (3H, s, 4-CH_3), 1.99 (3H, s, 5-CH_3), 2.12 (3H, s, 3-CH_3), 3.51 (3H, s, 4″-OCH_3), 3.63 (6H, s, 3′-OCH_3), 3.81 (3H, s, 4′-OCH_3), 6.23 (2H, s, 2′-H), 6.54 (1H, s, *J* = 2.0 Hz, 2″-H), 6.55 (1H, dd, *J* = 6.2, 2.0 Hz, 6″-H), 6.64 (1H, d, *J* = 6.2 Hz, 5″-H), 7.31(4H, td, *J* = 7.2, 1.0 Hz, Ar-H), 7.38 (2H, tt, *J* = 7.2, 1.0 Hz, Ar-H), 7.62 (4H, d, *J* = 7.2 Hz, Ar-H). $\boldsymbol{\delta_C}$ (125 MHz; $CDCl_3$) 9.4 (5-CH_3), 10.3 (3-CH_3) 10.4 (4-CH_3), 19.7 (Si*C*(CH_3)$_3$), 26.5 (SiC(*C*H_3)$_3$), 55.5 (4″-OCH_3), 55.9 (3′-OCH_3), 60.8 (4′-OCH_3), 107.4 (C-2′), 111.5 (C-5″), 114.5 (C-4), 115.9 (C-3), 120.7 (C-2″), 121.8 (C-6″), 126.7 (C-5), 127.6 (C-Ar), 128.7 (C-1′), 129.6 (C-1), 129.5 (C-2), 129.7 (C-Ar), 132.3 (C-1″), 133.0 (C-Ar), 136.0 (C-4′), 144.8 (C-3″), 149.8 (C-4″), 152.6 (C-3′). **IR**: (film)/cm-1; 2927, 2369, 1736, 1579, 1466, 1269, 1127, 1014, 907, 731. **m/z** (ESI+) 635 (MNa^+, 100%). **HRMS** (ESI+) Found (MNa^+): 658.2977; $C_{39}H_{45}NNaO_5Si$ requires 658.2959.

4.2.4.14 2-(4′-Methoxyphenyl)-4,5-dimethyl-1,3-diphenyl-1H-pyrrole ***8o***. Using diketone **1e**. Flash chromatography using 19:1 hexanes, ethyl acetate to yield 39 mg, 61% as a yellow foam. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.85. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 2.12 (6H, s, 2-CH_3, 3-CH_3), 3.65 (3H, s, OCH_3), 6.54 (2H, d, *J* = 6.8 Hz, 3′-H), 6.79 (2H, d, *J* = 6.8 Hz, 2′-H), 7.10–7.22 (10 H, m, Ar-H). $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 10.3 (4-CH_3), 11.0 (5-CH_3), 54.9 (OCH_3), 113.0 (C-3′), 114.1 (C-4), 122.9 (C-1′), 125.2 (C-5, Ar-CH), 126.4 (C-2), 126.9, 127.8, 128.6, 128.8 (Ar-CH), 129.8 (C-3), 130.5, 131.9 (Ar-CH), 136.5 (Ar-C), 139.3 (Ar-C), 157.6 (C-4′). **IR:** ν_{max}(film)/cm^{-1}; 2971, 2919, 1598, 1510, 1497, 1246, 1048, 835, 732, 699. ***m/z*** (ESI^+) 376 (MNa^+, 100%), 368 (15), 365 (20), 360 (25), 352 (85). **HRMS** (ESI^+) found (MNa^+): 376.1672; $C_{25}H_{23}NNaO$ requires 376.1675.

4.2.4.15 1-Benzyl-2-(4′-methoxyphenyl)-4,5-dimethyl-3-phenyl-1H-pyrrole ***8p***. Using diketone **1e**. Flash chromatography using 2:1 hexanes, ethyl acetate to yield 10 mg, 39% as a pink oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.87. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 2.03 (6H, s, 4-CH_3 and 5-CH_3), 3.66 (3H, s, OCH_3), 4.94 (2H, s, CH_2), 6.63 (2H, d, *J* = 8.4 Hz, 3′-H), 6.88 (2H, d, *J* = 7.2 Hz, Ar-H), 6.94 (2H, d, *J* = 8.4 Hz, 2′-H), 7.03–7.17 (8H, m, Ar-H). $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 10.2 (4-CH_3), 10.4 (5-CH_3), 47.6 (CH_2Ar), 55.1 (OCH_3), 113.5 (C-3′), 113.7 (C-5), 122.4 (C-2), 124.9, 125.3, 125.4, 125.8, 126.8, 127.7, 128.6, 130.0, 130.3, 132.2 136.7, 139.3 (Ar-CH), 158.5 (C-4′). **IR:** ν_{max}(film)/cm^{-1}; 2927, 2857, 1647, 1510, 1454, 1247, 730, 699. ***m/z*** (ESI^+) 382 (15), 354 (15), 332 (100), 354 (15), 368 (MH^+, 10%). **HRMS** (ESI^+) found (MH^+): 368.2019; $C_{26}H_{26}NO$ requires 368.2009.

4.2.4.16 5-(4′-Methoxyphenyl)-3-methyl-1-phenethyl-4-phenyl-1H-pyrrole-2-carbaldehyde ***8q***. Using diketone **1e**. Flash chromatography using 4:1 hexanes, ethyl acetate to yield 22 mg, 43% as a dark orange oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.69. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 2.31 (3H, s, 3-CH_3), 2.83 (2H, t, *J* = 7.6 Hz, 1-$CH_2C\mathit{H}_2$Ar), 3.72 (3H, s, OCH_3), 4.34 (2H, t, *J* = 7.6 Hz, 1-$C\mathit{H}_2CH_2$Ar), 6.71 (2H, d, *J* = 8.8 Hz, 3′-H), 6.83 (2H, d, *J* = 8.8 Hz, 2′-H), 6.91–6.95 (5H, m, 1-CH_2CH_2Ar-*H*), 7.09–7.18 (5H, m, Ar-H), 9.82 (CHO). $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 9.8 (3-CH_3), 37.8 (1-*C*H_2CH_2Ar), 47.5 (1-CH_2*C*H_2Ar), 55.2 (OCH_3), 113.7 (C-3′), 122.6 (C-1′), 126.1, 126.4 (Ar-CH), 127.2 (C-3), 127.9, 128.4, 128.6, 128.9, 130.3 (Ar-CH), 131.8 (C-2′), 133.1 (C-2), 134.2 (C-4), 138.3 (1-CH_2CH_2Ar-*C*, Ar-C), 141.0 (C-5), 159.6 (C-4′), 177.8 (CHO). **IR:** ν_{max}(neat)/cm^{-1}; 2966, 2841, 1646, 1456, 1250, 1176, 703. ***m/z*** (ESI^+) 418 (MNa^+, 100%), 333 (60). **HRMS** (ESI^+) found (MNa^+): 418.1781; $C_{27}H_{25}NNaO_2$ requires 418.1778.

4.2.4.17 5-(4′-Methoxyphenyl)-3-methyl-4-phenyl-1-(3″-phenylpropyl)-1H-pyrrole-2-carbaldehyde ***8r***. Using diketone **1e**. Flash chromatography using 9:1 hexanes, ethyl acetate to yield 26 mg, 55% as a viscous orange oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.72. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 1.85–1.91 (2H, m, 2″-H), 2.28 (3H, s, 3-CH_3), 2.36 (2H, t, *J* = 8.0 Hz, 3″-H), 3.73 (3H, s, OCH_3), 4.19 (2H, t, *J* = 7.6 Hz, 1″-H), 6.71 (2H, d, *J* = 8.8 Hz, 3′-H), 6.93–7.17 (12H, m, 2′-H, Ar-H), 9.76 (1H, s, CHO). $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 9.8 (3-CH_3), 32.6 (C-2″), 32.8 (C-3″), 45.5 (C-1″), 55.2 (OCH_3), 113.9 (C-3′), 122.7 (C-1′), 125.7, 126.1 (Ar-CH), 127.4 (C-3), 127.2, 128.1, 128.2, 130.3 (Ar-CH), 131.8 (C-2′), 132.2 (C-2), 132.8 (C-4), 134.2 (Ar-C), 140.6 (C-5), 141.2 (3″-Ar-C), 159.6 (C-4′), 177.8 (CHO). **IR:** ν_{max}(film)/cm^{-1}; 2961, 2854, 1645, 1455, 1248, 1174, 802, 789, 700. ***m/z*** (ESI^+) 432 (MNa^+, 100%), 281 (25). **HRMS** (ESI^+) found (MNa^+): 432.1930; $C_{28}H_{27}NNaO_2$ requires 432.1934.

4.2.4.18 2-Butyl-4,5-dimethyl-1,3-diphenyl-1H-pyrrole ***8s***. Using diketone **1f**. Flash chromatography using 2:1 hexanes, ethyl acetate to yield 14 mg, 71% as a yellow oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.63. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 0.49 (3H, t, *J* = 7.6 Hz, 2-$CH_2CH_2CH_2C\mathit{H}_3$), 0.89 (2H, sext., *J* = 7.6 Hz, 2-$CH_2CH_2C\mathit{H}_2CH_3$), 1.02 (2H, pent., *J* = 7.6 Hz, 2-$CH_2C\mathit{H}_2CH_2CH_3$), 1.91 (3H, s, 5-$CH_3$), 1.95 (3H, s, 4-$CH_3$), 2.36 (2H, t, *J* = 7.6 Hz, 2-$C\mathit{H}_2CH_2CH_2CH_3$), 7.14–7.40 (10H, m, Ar-H). $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 10.1 (4-CH_3), 10.7 (5-CH_3), 13.4 (2-$CH_2CH_2CH_2\mathit{C}H_3$), 22.1 (2-$CH_2CH_2\mathit{C}H_2CH_3$), 24.5 (2-$CH_2\mathit{C}H_2CH_2CH_3$), 32.3 (2-*C*$H_2CH_2CH_2CH_3$), 122.8 (C-4), 122.0 (C-2), 124.7 (C-5), 125.4, 127.6, 127.9, 128.7, 128.9, 129.7 (Ar-CH), 130.1 (C-3), 137.1, 139.3 (Ar-C). **IR:** ν_{max}(film)/cm^{-1}; 2957, 2859, 1598, 1497, 1260, 801, 755, 699. ***m/z*** (ESI^+) 304 (MH^+, 100%), 302 (90), 301 (80). **HRMS** (ESI^+) found (MH^+): 304.2047; $C_{22}H_{26}N$ requires 304.2060.

4.2.4.19 5-Butyl-3-methyl-4-phenyl-1-(3″-phenylpropyl)-1H-pyrrole-2-carbaldehyde ***8t***. Using diketone **1f**. Flash chromatography using 9:1 hexanes, ethyl acetate to yield 32 mg, 44% as a yellow oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.66. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 0.73 (3H, t, *J* = 7.2 Hz, 5-$CH_2CH_2CH_2C\mathit{H}_3$), 1.11–1.16 (2H, m, 5-$CH_2CH_2$-$C\mathit{H}_2CH_3$), 1.26–1.33 (2H, m, 5-$CH_2C\mathit{H}_2CH_2CH_3$), 2.03–2.09 (2H, m, 2″-H), 2.25 (3H, s, 3-CH_3), 2.39 (2H, t, *J* = 8.0

Hz, 5-C*H*$_2$CH$_2$CH$_2$CH$_3$), 2.72 (2H, t, *J* = 7.6 Hz, 3″-H), 4.27 (2H, t, *J* = 8.0 Hz, 1″-H), 7.16–7.40 (10H, m, Ar-H), 9.68 (1H, s, CHO). **δ$_C$** (100 MHz; CDCl$_3$) 9.5 (3-CH$_3$), 13.5 (5-CH$_2$CH$_2$CH$_2$*C*H$_3$), 22.5 (5-CH$_2$CH$_2$*C*H$_2$CH$_3$), 23.9 (5-*C*H$_2$CH$_2$CH$_2$CH$_3$), 31.9 (5-CH$_2$*C*H$_2$CH$_2$CH$_3$), 32.9 (C-3″), 33.1 (C-2″), 44.9 (C-1″), 124.8 (C-5), 126.0, 126.6, 128.3, 128.4, 130.2 (Ar-CH), 130.6 (C-3), 133.1 (C-4), 134.8 (Ar-C), 141.0 (C-2), 141.3 (3″-Ar-C), 176.8 (CHO). **IR:** ν$_{max}$(film)/cm^{-1}; 2958, 2862, 1709, 1644, 1496, 1454, 750, 701. ***m/z*** (ESI$^+$) 360 (MNa$^+$, 100%). **HRMS** (ESI$^+$) found (MH$^+$): 360.2312; $C_{25}H_{30}NO$ requires 360.2322.

4.2.4.20 (S)-5-(4′-Methoxyphenyl)-3-methyl-1-(1″-phenylethyl)-4-propyl-1H-pyrrole-2-carbaldehyde ***8u***. Using diketone **1g**. Flash chromatography using 4:1 hexanes, ethyl acetate to yield 9 mg, 30% as a yellow oil. **α$_D$** = +17 (*c* = 1.3, CHCl$_3$). **R$_F$** (2:1 hexanes, ethyl acetate) = 0.85. **δ$_H$** (300 MHz; CDCl3; Me$_4$Si) 0.79 (3H, t, *J* = 7.6 Hz, CH$_2$CH$_2$C*H*$_3$), 1.35 (2H, pent., *J* = 7.6 Hz, CH$_2$C*H*$_2$CH$_3$), 1.78 (3H, d, *J* = 7.1 Hz, 1-CH(C*H*$_3$)Ar), 2.20–2.25 (2H, m, C*H*$_2$CH$_2$CH$_3$), 2.36 (3H, s, 3-CH$_3$), 3.82 (3H, s, 4′-OCH$_3$), 5.82 (1H, br s, 1-C*H*(CH$_3$)Ar), 6.86 (2H, d, *J* = 7.5 Hz, 3′-H), 6.98–7.01 (2H, m, Ar-H), 7.17–7.25 (5H, m, 2′-H, Ar-H), 9.57 (1H, s, CHO). **δ$_C$** (75 MHz; CDCl$_3$) 10.1 (3-CH$_3$), 14.0 (CH$_2$CH$_2$*C*H$_3$), 19.7 (1-CH(*C*H$_3$)Ar), 24.0 (CH$_2$*C*H$_2$CH$_3$), 26.2 (*C*H$_2$CH$_2$CH$_3$), 54.1 (1-*C*H(CH$_3$)Ar), 55.3 (4′-OCH$_3$), 133.8 (C-3′), 123.9 (C-1′, C-4), 125.7 (Ar-CH), 126.7 (Ar-CH, C-2), 128.2 (Ar-CH), 131.6 (C-2′, C-3), 142.3 (C-5, Ar-C), 159.7 (C-4′), 177.9 (CHO). **IR:** ν$_{max}$(film)/cm^{-1}; 2926, 2855, 1597, 1501, 1251, 1139, 1026, 763, 699. **m/z** (ESI+) 384 (MNa$^+$, 100 %), 365 (20). **HRMS** (ESI$^+$): found (MNa$^+$): 384.1946; $C_{24}H_{27}NNaO_2$ requires 384.1934.

4.2.4.21 2-(Benzo[d][1″,3″]dioxol-5″-yl)-3-(benzo[d][1′,3′]dioxol-5′-ylmethyl)-1-(4‴-bromo-2‴-fluorophenyl)-4,5-dimethyl-1H-pyrrole ***8v***. Using diketone **1h**. Flash chromatography using 14:1 hexanes, ethyl acetate to yield 14 mg, 24% as a colourless oil. **R$_F$** (2:1 hexanes, ethyl acetate) = 0.79. **δ$_H$** (400 MHz; CDCl$_3$; Me$_4$Si) 1.89 (3H, s, 4-CH$_3$), 1.98 (3H, s, 5-CH$_3$), 3.73 (2H, d, *J* = 5.1 Hz, 3-CH$_2$), 5.88, 5.90 (4H, s, 2′-H, 2″-H), 6.49–6.51 (2H, m, 4′-H, 6′-H), 6.60–6.62 (2H, m, 6″-H, 7′-H), 6.69–6.72 (2H, m, 4″-H, 7″-H), 6.93 (1H, t, *J* = 8.3 Hz, 3‴-H), 7.19–7.22 (1H, m, 5‴-H), 7.28 (1H, dd, *J* = 2.1, 9.0 Hz, 6‴-H). **δ$_C$** (100 MHz; CDCl$_3$) 9.6 (4-CH$_3$), 10.2 (5-CH$_3$), 30.4 (3-CH$_2$), 100.7, 100.9 (C-2′, C-2″), 108.5 (C-4″, C-7″), 108.7 (C-7′), 110.2 (C-4′), 115.5 (C-4), 119.8, 119.9, 120.1 (C-6‴, C-4‴, C-3), 120.8 (C-6″), 123.6 (C-6′), 126.2, 126.6, 127.0 (C-5, C-5″, C-1‴), 127.6 (C-5‴), 130.9 (C-5′), 132.0 (C-3‴), 136.0 (C-2), 145.3, 146.4, 147.2, 147.5 (C-7a′, C-3a′, C-7a″, C-3a″), 159.4 (C-2‴). **IR:** ν$_{max}$(film)/cm^{-1}; 2895, 1499, 1485, 1443, 1229, 1040, 813, 734. ***m/z*** (ESI$^+$) 544 (MNa$^+$, 30%), 405 (100). **HRMS** (ESI$^+$) found (MNa$^+$): 544.0510; $C_{27}H_{21}BrFNNaO_4$ requires 544.0530.

4.2.4.22 4‴-(2-(Benzo[d][1″,3″]dioxol-5″-yl)-3-(benzo[d][1′,3′]dioxol-5′-ylmethyl)-4,5-dimethyl-1H-pyrrol-1-yl)benzenesulfonamide ***8w***. Using diketone **1h**. Flash chromatography using 14:1 hexanes, ethyl acetate to yield 8.2 mg, 15% as a colourless oil. **R$_F$** (2:1 hexanes, ethyl acetate) = 0.20. **δ$_H$** (400 MHz; CDCl$_3$; Me$_4$Si) 1.91 (3H, s, 4-CH$_3$), 2.07 (3H, s, 5-OCH$_3$), 3.74 (2H, s, 3-CH$_2$), 5.00 (2H, s, NH$_2$), 5.88, 5.90 (4H, s, 2′-H, 2″-H), 6.45–6.48 (2H, m, 4′-H, 6′-H), 6.60–6.62 (2H, m, 6″-H, 7′-H), 6.45–6.48 (2H, m, 4″-H, 7″-H), 7.19 (2H, d, *J* = 8.6 Hz, 2‴-H), 7.84 (2H, d, *J* = 8.6 Hz, 3‴-H). **δ$_C$** (100 MHz; CDCl$_3$) 9.7 (4-CH$_3$), 11.2 (5-CH$_3$), 30.4 (3-CH$_2$), 100.7, 100.9 (C-2′, C-2″), 108.0 (C-4″, C-7″), 108.1 (C-7′), 110.5 (C-4′), 116.3 (C-4), 120.8 (C-6″), 124.0 (C-6′), 126.2 (C-3), 127.0 (C-5″), 127.1 (C-3‴), 128.6 (C-5), 128.7 (C-2‴), 130.3 (C-5′), 135.8 (C-2), 139.5 (C-1‴), 143.6 (C-4‴), 145.4, 146.4, 147.3, 147.5 (C-7a′, C-3a′, C-7a″, C-3a″). **IR:** ν$_{max}$(film)/cm^{-1}; 3377, 2920, 1501, 1486, 1442, 1247, 1165, 1038, 811, 731. The sample decomposed prior to mass spectrum acquision.

4.2.4.23 4‴-(3-(Benzo[d][1′,3′]dioxol-5′-ylmethyl)-2-(4″-methoxyphenyl)-4,5-dimethyl-1H-pyrrol-1-yl)benzenesulfonamide ***8x***. Using diketone **1i**. Flash chromatography using 14:1 hexanes, ethyl acetate to yield 16 mg, 29% as a yellow oil. **R$_F$** (2:1 hexanes, ethyl acetate) = 0.20. **δ$_H$** (400 MHz; CDCl$_3$; Me$_4$Si) 1.92 (3H, s, 4-CH$_3$), 2.08 (3H, s, 5-CH$_3$), 3.72 (2H, s, 3-CH$_2$), 3.73 (3H, s, OCH$_3$), 4.92 (2H, s, NH$_2$), 5.90 (2H, s, 2′-H), 6.62–6.63 (2H, m, 6′-H, 7′-H), 6.68–6.72 (3H, m, 3″-H, 4′-H), 6.89 (2H, d, *J* = 8.8 Hz, 2″-H), 7.17 (2H, d, *J* = 8.4 Hz, 2‴-H), 7.81 (2H, d, *J* = 8.4 Hz, 3‴-H). **δ$_C$** (100 MHz; CDCl$_3$) 9.7 (4-CH$_3$), 11.0 (5-CH$_3$), 30.4 (3-CH$_2$), 55.1 (OCH$_3$), 100.7 (C-2′), 108.0 (C-4′), 108.7 (C-7′), 113.6 (C-3″), 116.3 (C-4), 120.4 (C-3), 120.8 (C-6′), 124.8 (C-1″), 125.7 (C-5), 127.0 (C-3‴), 128.8 (C-2‴), 130.4 (C-5′), 131.3 (C-2″), 136.0 (C-2), 139.4 (C-4‴), 143.6 (C-1‴), 145.4, 147.5 (C-7a′, C-3a′), 158.2 (C-4″). **IR:** ν$_{max}$(film)/cm^{-1}; 3267, 2917, 1596, 1499, 1487, 1245, 1162, 837, 730. ***m/z*** (ESI$^+$) 513 (MNa$^+$, 10%), 391 (100). **HRMS** (ESI$^+$) found (MNa$^+$): 513.1449; $C_{27}H_{26}N_2NaO_5S$ requires 513.1455.

4.2.4.24 2-(3′-isopropoxy-4′-methoxyphenyl)-1-(4″-methoxybenzyl)-4,5-dimethyl-1H-pyrrole ***8y***. Using diketone **1j**. Flash chromatography using 9:1 hexanes, ethyl acetate to yield 88 mg, 59% as a yellow oil. **R$_F$** = 0.81 (2:1 hexanes, ethyl acetate). **δ$_H$** (500 MHz; CDCl$_3$; Me$_4$Si) 1.21 (6H, d, *J* = 6.2 Hz, CH(C*H*$_3$)$_2$), 2.07 (3H, s, 4-CH$_3$), 2.09 (3H, s, 5-CH$_3$), 3.78 (3H, s, 4″-OCH$_3$), 3.83 (3H, s, 4′-OCH$_3$), 4.14–4.19 (1H, m, C*H*(CH$_3$)$_2$), 5.02 (2H, s, 1-CH$_2$), 6.05 (1H, s, 3-CH), 6.77 (1H, s, *J* = 2.0 Hz, 2′-H), 6.80 (1H, d, *J* = 8.2 Hz, 5′-H), 6.82 (1H, dd, *J* = 2.0, 8.2 Hz, 6′-H), 6.83 (2H, dd, *J* = 2.0, 10.4 Hz, 3″-H), 6.88 (2H, dd, *J* = 2.0, 10.4 Hz, 2″-H). **δ$_C$** (125 MHz; CDCl$_3$) 10.0 (4-CH$_3$), 11.3 (5-CH$_3$), 22.0 (3′-OCH(*C*H$_3$)$_2$), 47.2 (1-CH$_2$), 55.3 (4″-OCH$_3$), 55.9 (4′-OCH$_3$), 70.9 (3′-O*C*H(CH$_3$)$_2$), 108.9 (C-3), 111.8 (C-5′), 114.1 (C-3″), 114.9 (C-4), 115.9 (C-2′), 121.2 (C-6′), 125.9 (C-5), 126.6 (C-1′), 126.8 (C-2″), 131.6 (C-1″), 133.2 (C-2), 146.9 (C-3′), 149.2 (C-4′), 158.6 (C-4″). **IR**: (film)/cm-1; 2974, 1611, 1585, 1524, 1245, 1174, 1032, 959, 813, 787. **m/z** (ESI+) 402 (MNa$^+$, 100%). **HRMS** (ESI+) Found (MNa$^+$): 402.2027; $C_{24}H_{29}NNaO_3$ requires 402.2040.

4.2.4.25 2-(3′-isopropoxy-4′-methoxyphenyl)-1-(4″-methoxyphenyl)-4,5-dimethyl-1H-pyrrole ***8z***. Using diketone **1j**. Flash chromatography using 9:1 hexanes, ethyl acetate to yield 53 mg, 41% as a yellow oil. $\mathbf{R_F}$ = 0.67 (2:1 hexanes, ethyl acetate). $\boldsymbol{\delta_H}$ (500 MHz; $CDCl_3$; Me_4Si) 1.16 (6H, d, *J* = 6.2 Hz, 3′-OCH(C*H*$_3$)$_2$), 2.02 (3H, s, 4-CH_3), 2.12 (3H, s, 5-CH_3), 3.78 (3H, s, 4′-OCH_3), 3.79 (3H, s, 4″-OCH_3), 4.11–4.14 (1H, m, 3′-OC*H*(CH_3)$_2$), 6.16 (1H, s, 3-CH), 6.50 (1H, d, *J* = 2.0 Hz, 2′-H), 6.69 (1H, d, *J* = 8.2 Hz, 5′-H), 6.73 (1H, dd, *J* = 2.0, 8.2 Hz, 6′-H), 6.87 (2H, dd, *J* = 2.4, 8.8 Hz, 3″-H), 7.07 (2H, d, *J* = 2.4, 8.8 Hz, 2″-H). $\boldsymbol{\delta_C}$ (125 MHz; $CDCl_3$) 10.8 (4-CH_3), 11.3 (5-CH_3), 22.0 (CH(*C*H_3)$_2$), 55.4 (4′-OCH_3), 55.9 (4″-OCH_3), 71.0 (*C*H(CH_3)$_2$), 109.3 (C-3), 111.6 (C-5′), 114.1 (C-3″), 115.0 (C-4), 115.7 (C-2′), 120.6 (C-6′), 126.5 (C-1′), 127.5 (C-5), 129.6 (C-2″), 132.7 (C-1″), 132.9 (C-2), 146.9 (C-3′), 149.2 (C-4′), 158.6 (C-4″). **IR**: (film)/cm-1; 2973, 1512, 1490, 1245, 1168, 1032, 998, 729. **m/z** (ESI+) 388 (MNa^+, 100%). **HRMS** (ESI+) Found (MNa^+): 388.1870; $C_{23}H_{27}NNaO_3$ requires 388.1883.

4.2.4.26 1-benzyl-5-(3′-isopropoxy-4′-methoxyphenyl)-2,3-dimethyl-1H-pyrrole ***8aa***. Using diketone **1j**. Flash chromatography using 9:1 hexanes, ethyl acetate 42 mg, 30% as a yellow oil. $\mathbf{R_F}$ = 0.83 (2:1 hexanes, ethyl acetate). $\boldsymbol{\delta_H}$ (500 MHz; $CDCl_3$; Me_4Si) 1.17 (6H, d, *J* = 6.1 Hz, 3′-OCH(C*H*$_3$)$_2$), 2.06 (3H, s, 3-CH_3), 2.10 (3H, s, 2-CH_3), 3.82 (3H, s, 4′-OCH_3), 4.08–4.13 (1H, m, 3′-OC*H*(CH_3)$_2$), 5.07 (2H, s, 1-CH_2), 6.06 (1H, s, 4-H), 6.73 (1H, d, *J* = 2.0 Hz, 2′-H), 6.79 (1H, d, *J* = 8.4 Hz, 5′-H), 6.83 (1H, dd, *J* = 2.0, 8.4 Hz, 6′-H), 6.97 (2H, dd, *J* = 1.0, 7.2 Hz, 2″-H), 7.19 (1H, td, *J* = 1.0, 7.2 Hz, 4″-H). $\boldsymbol{\delta_C}$ (125 MHz; $CDCl_3$) 10.0 (3-CH_3), 11.3 (2-CH_3), 22.0 (3′-OCH(*C*H_3)$_2$), 47.8 (1-CH_2), 56.0 (4′-OCH_3), 70.9 (3′-O*C*H(CH_3)$_2$), 108.9 (C-4), 111.9 (C-5′), 114.9 (C-3), 115.8 (C-2′), 121.1 (C-6′), 125.6 (C-2″), 125.7 (C-2), 126.5 (C-1′), 126.8 (C-4″), 128.7 (C-3″), 133.2 (C-5), 139.5 (C-1″), 146.9 (C-3′), 149.1 (C-4′). **IR**: (film)/cm-1; 2923, 2855, 1605, 1525, 1494, 1246, 1137, 1029, 908, 730. **m/z** (ESI+) 372 (MNa^+, 100%). **HRMS** (ESI+) Found (MNa^+): 372.1920; $C_{23}H_{27}NNaO_2$ requires 372.1934.

4.2.4.27 2-(4′-Methoxyphenyl)-3,5-dimethyl-1-phenyl-1H-pyrrole ***8ab***. Using diketone **1k**. Flash chromatography using 14:1 hexanes, ethyl acetate to yield 11 mg, 30% as a pink oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.83. $\boldsymbol{\delta_H}$ (300 MHz; $CDCl_3$; Me_4Si) 2.12 (3H, s, 3-CH_3), 2.13 (3H, s, 5-CH_3), 3.74 (3H, s, OCH_3), 5.94 (1H, s, 4-H), 6.71 (2H, d, *J* = 8.8 Hz, 3′-H), 6.95 (2H, d, *J* = 8.8 Hz, 2′-H), 7.05–7.07 (2H, m, Ar-H), 7.23–7.24 (3H, m, Ar-H). $\boldsymbol{\delta_C}$ (75 MHz; $CDCl_3$) 11.9 (3-CH_3), 13.1 (5-CH_3), 55.1 (OCH_3), 109.3 (C-4), 113.2 (C-3′), 116.2 (C-3), 125.6 (C-1′), 126.8, 128.4, 128.6 (Ar-CH), 129.2 (C-5), 131.2 (C-2′), 131.4 (C-2), 139.5 (Ar-C), 157.6 (C-4′). **IR:** ν_{max}(film)/cm^{-1}; 2923, 2855, 1497, 1259, 1245, 1020, 798, 759, 732, 698. ***m/z*** (ESI^+) 257 (100), 278 (MH^+, 10%). **HRMS** (ESI^+) found (MH^+): 278.1504; $C_{19}H_{20}NO$ requires 278.1539.

4.2.4.28 5-(4′-Methoxyphenyl)-4-methyl-1-(3″-phenylpropyl)-1H-pyrrole-2-carbaldehyde ***8ac***. Using diketone **1k**. Flash chromatography using 9:1 hexanes, ethyl acetate to yield 5.0 mg, 13% as a purple oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.79. $\boldsymbol{\delta_H}$ (300 MHz; $CDCl_3$; Me_4Si) 1.88 (2H, pent., *J* = 7.7 Hz, 2″-H), 1.97 (3H, s, 4-CH_3), 2.45 (2H, t, *J* = 7.7 Hz, 3″-H), 3.73 (3H, s, OCH_3), 4.21 (2H, t, *J* = 7.7 Hz, 1″-H), 6.81 (1H, s, 3-H), 6.93 (2H, d, *J* = 8.8 Hz, 3′-H), 6.99 (1H, s, Ar-H), 7.12–7.21 (6H, m, Ar-H, 2′-H), 9.47 (1H, s, CHO). $\boldsymbol{\delta_C}$ (75 MHz; $CDCl_3$) 11.5 (4-CH_3), 32.6 (C-2″), 32.7 (C-3″), 45.6 (C-1″), 55.3 (OCH_3), 114.1 (C-3′), 119.3 (C-3), 122.8 (C-1′), 125.7, 128.2, 128.4 (Ar-CH), 128.6, 128.8 (C-2, C-4), 131.3 (C-2′), 141.2 (C-5, Ar-C), 159.7 (C-4′), 178.6 (CHO). **IR:** ν_{max}(neat)/cm^{-1}; 3025, 2921, 2853, 1655, 1459, 1454, 1418, 1250, 1036, 1176, 748, 698. ***m/z*** (ESI^+) 356 (MNa^+, 100%), 352 (20), 301 (80), 245 (50). **HRMS** (ESI^+) found (MNa^+): 356.1620; $C_{22}H_{23}NNaO_2$ requires 356.1621.

4.2.4.29 2-(4′-Methoxyphenyl)-5-methyl-1,3-diphenyl-1H-pyrrole ***8ad***. Using diketone **1m**. Flash chromatography using 9:1 hexanes, ethyl acetate to yield 13 mg, 30% as a yellow oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.62. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 2.08 (3H, s, 5-CH_3), 3.65 (3H, s, OCH_3), 6.22 (1H, s, 4-H), 6.56 (2H, d, *J* = 8.8 Hz, 3′-H), 6.85 (2H, d, *J* = 8.8 Hz, 2′-H), 7.01–7.04 (4H, m, Ar-H), 7.10–7.23 (6H, m, Ar-H). $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 13.1 (5-CH_3), 55.0 (OCH_3), 107.6 (C-4), 113.3 (C-3′), 121.9 (C-3), 125.0 (Ar-CH), 125.4 (C-1′), 127.2, 128.0, 128.6, 128.7 (Ar-CH, C-2′), 130.0 (C-2, C-5), 132.2 (C-4′). **IR:** ν_{max}(film)/cm^{-1}; 2933, 2964, 2855, 1599, 1508, 1250, 1031, 1175, 836, 761, 699. ***m/z*** (ESI^+) 362 (MNa^+, 10%), 360 (40), 319 (50), 298 (100). **HRMS** (ESI^+) found (MNa^+): 362.1511; $C_{24}H_{21}NNaO$ requires 362.1515.

4.2.4.30 4″-(2-(Benzo[d][1′,3′]dioxol-5′-yl)-3,5-dimethyl-4-phenyl-1H-pyrrol-1-yl)benzenesulfonamide ***8ae***. Using diketone **1n**. Flash chromatography using 14:1 hexanes, ethyl acetate to yield 19 mg, 82% b.r.s.m. as a yellow oil. $\mathbf{R_F}$ (2:1 hexanes, ethyl acetate) = 0.28. $\boldsymbol{\delta_H}$ (400 MHz; $CDCl_3$; Me_4Si) 2.07 (3H, s, 3-CH_3), 2.14 (3H, s, 5-CH_3), 4.84 (2H, br s, NH_2), 5.93 (2H, s, 2′-H), 6.53–6.57 (2H, m, 6′-H, 7′-H), 6.68 (1H, d, *J* = 8.0 Hz, 4′-H), 7.26–7.29 (2H, m, 2″-H), 7.37–7.45 (5H, m, Ar-H), 7.88 (2H, d, *J* = 8.7 Hz, 3″-H). $\boldsymbol{\delta_C}$ (100 MHz; $CDCl_3$) 11.2 (3-CH_3), 12.3 (5-CH_3), 101.0 (C-2′), 108.1 (C-4′), 110.6 (C-7′), 117.0 (C-3), 124.1 (C-6′), 126.0 (C-5′), 126.3 (Ar-CH and C-5), 127.2 (C-3″), 128.2 (Ar-CH), 128.7 (C-2, C-2″), 130.0 (Ar-CH), 130.1 (C-4), 135.9 (Ar-C), 139.8 (C-1″), 143.4 (C-4″), 146.2, 147.3 (C-7a′, C-3a′). ***m/z*** (ESI^-) 445 (MH^-, 90%), 441 (100). **HRMS** (ESI^-) found (MH^-): 445.1190; $C_{25}H_{21}N_2O_4S$ requires 445.1228.

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References.

(1) Artico, M.; Di Santo, R.; Costi, R.; Massa, S.; Retico, A.; Artico, M.; Apuzzo, G.; Simonetti, G.; Strippoli, V. *J. Med. Chem.* **1995**, *38*, 4223–4233.
(2) Carbone, A.; Pennati, M.; Parrino, B.; Lopergolo, A.; Barraja, P.; Montalbano, A.; Spanò, V.; Sbarra, S.; Doldi, V.; De Cesare, M.; Cirrincione, G.; Diana, P.; Zaffaroni, N. *J. Med. Chem.* **2013**, *56*, 7060–7072.
(3) Chaniyara, R.; Tala, S.; Chen, C.-W.; Zang, X.; Kakadiya, R.; Lin, L.-F.; Chen, C.-H.; Chien, S.-I.; Chou, T.-C.; Tsai, T.-H.; Lee, T.-C.; Shah, A.; Su, T.-L. *J. Med. Chem.* **2013**, *56*, 1544–1563.
(4) Jiang, S.; Lu, H.; Liu, S.; Zhao, Q.; He, Y.; Debnath, A. K. *Antimicrob. Agents Chemother.* **2004**, *48*, 4349–4359.
(5) Sharma, L.; Sattigeri, J. A.; Kumar, N.; Yadav, A.; Momin, R.; Ahmed, S.; Cliffe, I. A.; Bhatnagar, P. K.; Ghosh, S.; Raj, V. S.; Upadhyay, D. J. WO2010013222 A1, February 4, 2010.
(6) Pacorel, B.; Leung, S. C.; Stachulski, A. V.; Davies, J.; Vivas, L.; Lander, H.; Ward, S. A.; Kaiser, M.; Brun, R.; O'Neill, P. M. *J. Med. Chem.* **2010**, *53*, 633–640.
(7) Roth, B. D. *Prog. Med. Chem.* **2002**, *40*, 1–22.
(8) Wang, W. D.; Gao, X.; Strohmeier, M.; Wang, W.; Bai, S.; Dybowski, C. *J. Phys. Chem. B* **2012**, *116*, 3641–3649.
(9) Maggon, K. *Drug Discov. Today* **2005**, *10*, 739–742.
(10) LAMATTINA, J. *Chem. Eng. News Arch.* **2009**, *87*, 61–63.
(11) Delbaldo, C.; Faivre, S.; Dreyer, C.; Raymond, E. *Ther. Adv. Med. Oncol.* **2012**, *4*, 9–18.
(12) Blumenthal, G. M.; Cortazar, P.; Zhang, J. J.; Tang, S.; Sridhara, R.; Murgo, A.; Justice, R.; Pazdur, R. *The Oncologist* **2012**, *17*, 1108–1113.
(13) Khaghaninejad, S.; Heravi, M. M. In *Advances in Heterocyclic Chemistry*; Alan R. Katritzky, Ed.; Academic Press, 2014; Vol. 111, pp 95–146.
(14) Amarnath, V.; Anthony, D. C.; Amarnath, K.; Valentine, W. M.; Wetterau, L. A.; Graham, D. G. *J. Org. Chem.* **1991**, *56*, 6924–6931.
(15) Barker, D.; Dickson, B.; Dittrich, N.; Rye, C. E. *Pure Appl. Chem.* **2012**, *84*, 1557+.
(16) Dickson, B. D.; Dittrich, N.; Barker, D. *Tetrahedron Lett.* **2012**, *53*, 4464–4468.
(17) Rye, C.; Barker, D. *Synlett* **2009**, 3315–3319.
(18) Rye, C. E.; Barker, D. *J. Org. Chem.* **2011**, *76*, 6636–6648.
(19) Davidson, S. J.; Barker, D. *Tetrahedron Lett.* **2015**, *56*, 4549–4553.
(20) Yoon, T. P.; Dong, V. M.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **1999**, *121*, 9726–9727.
(21) Yoon, T. P.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2001**, *123*, 2911–2912.
(22) Jung, E.-K.; Dittrich, N.; Pilkington, L. I.; Rye, C.; Leung, E.; Barker, D. *Tetrahedron* **2015**, *71*, 9439-9456.
(23) Alberti, M. N.; Vougioukalakis, G. C.; Orfanopoulos, M. *J. Org. Chem.* **2009**, *74*, 7274–7282.
(24) Schmidt, E. Y.; Senotrusova, E. Y.; Ushakov, I. A.; Kazheva, O. N.; Dyachenko, O. A.; Alexandrov, G. G.; Ivanova, A. V.; Mikhaleva, A. I.; Trofimov, B. A. *ARKIVOC* **2010**, 352–359.
(25) Hanessian, S.; Chénard, E. *Org. Lett.* **2012**, *14*, 3222–3225.
(26) Matsumoto, T.; Katayama, N.; Mabuchi, H. WO0190067 (A1), November 29, 2001.

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