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Pd(0) catalyzed three–five-component C-2-arylallylation of active methylene heterocycles: pyrazolones, oxazolones, isoxazolones and *N*,*N*′-dimethylbarbituric acid

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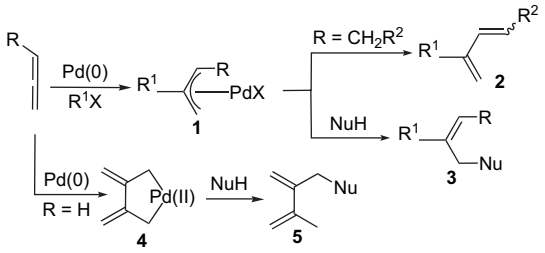
Abstract—A Pd(0) catalyzed three–five-component cascade involving an aryl iodide, allene and a heterocyclic pronucleophile is used to prepare 2-arylallyl derivatives (**10**–**12** and **16**–**24**) from 3-phenyl-5-isoxazolone (**6**) and 1-phenyl-3-methylpyrazolin-5-one (**7**) in moderate yield. Similar cascade allylation of masked amino acids 4-methyl-2-phenyl-4*H*-oxazol-5-one (**8a**), 4-benzyl-2-phenyl-4*H*-oxazol-5-one (**8b**) and 4-isopropyl-2-phenyl-4*H*-oxazol-5-one (**8c**) gave analogous products (**25**–**37**) in good yield. *N*,*N*-Dimethylbarbiturates (**38**–**49**) are similarly prepared from *N*,*N*-dimethylbarbituric acid (**9**) in excellent yield.

1. Introduction

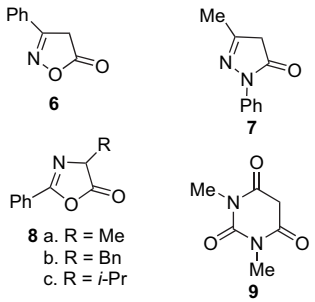
The regioselective addition of R^1PdX (R^1=aryl, vinyl) to allenes occurs at the centre C-atom furnishing π-allyl species **1**[1] (Scheme 1). In the absence of a nucleophile a slow β-hydride elimination can occur furnishing 1,3-dienes **2**, which can be trapped in situ in Diels–Alder reactions with appropriate dipolarophiles.[2] Generation of **1** in the presence of a range of *C*-, *N*-, *O*- and *S*-pronucleophiles affords the allylated derivatives **3**.[3] The parent allene, in the absence of an aryl/vinyl halide/triflate, reacts with Pd(0) catalysts, probably via oxidative cyclization to **4**, and is further processed by nucleophiles to afford the 1,3-dienes **5**. Substituted allenes do not appear to readily participate in this latter sequence.[4]



Scheme 1.

The rich chemistry inherent in Scheme 1 is an ongoing focus of aspects of our research. Thus appropriate five- and six-membered heterocycles, which are potentially bifunctional nucleophiles (*C*- vs *N*-, *O*- or *S*-pronucleophilic centres) offer opportunities to be decorated with a wide range of complex allyl substituents thus acting as useful scaffolds for drug discovery programs and combinatorial chemistry.

In a previous paper in this series, we described the use of coumarins/pyrones and a dihydropyrid-2-one as heterocyclic pronucleophiles[3a] for the formation of **3**. We now report related studies on the five-membered heterocycles **6**–**8** and *N*,*N*′-dimethylbarbituric acid **9**.



Substrates **6** and **7** offer opportunities to explore C- versus O-allylation whilst heterocycles **8a**–**c** are masked α-amino acids and are of interest as a source of novel α,α-disubstituted amino acids as well as, potentially, *C*- versus *O*-nucleophile. *N*,*N*′-Dimethylbarbituric acid **9** was selected as a substrate due to the continued medical use of barbiturates

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not only as anti-convulsants[5] but also, more recently, for their reported anti-cancer, analeptic, immunomodulating and anti-AIDS activity.[5–7]

2. Results and discussion

Our studies were initiated with 3-phenyl-5-isoxazolone (**6**). Reaction of **6**, allene (1 atm) and methyl 4-iodobenzoate in the presence of $Pd(OAc)_2$ (10 mol %), PPh_3 (20 mol %) and Cs_2CO_3 (2.0 mol equiv) in toluene at 100 °C over 2 h afforded a 1:2 mixture of *C*,*C*-diallylated product **12** and *C*,*O*-diallylated product **11** (Scheme 2). When the reaction temperature was decreased and/or the reaction time shortened a third product **10** was also observed.

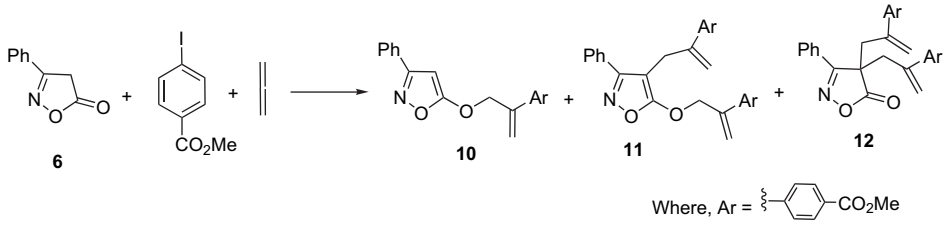
Table 1 summarizes the results of screening the catalyst system, base, solvent and reaction temperature, and demonstrates the sensitivity of the product profile to the reaction temperature, time and, to a lesser extent, solvent. At low temperature (40 °C) in DMF the conversion was incomplete even after 24 h but in all cases the *O*-allylated compound **10** was the sole product (Table 1, entries 9–11). Temperatures of 50–80 °C in toluene or MeCN favour the *C*,*O*-diallylated compound **11**. At these temperatures a solvent effect is also discernable with reactions in MeCN delivering a 1:2–1:4 mixture of **12** and **11** but no **10** (Table 1, entries 6–8) whilst in toluene 2:1 mixtures of **11** and **10** but no **12** are produced (Table 1, entries 1, 3 and 4). Extended reaction time at 70 °C in toluene results in a 1:2:1 mixture of **12**, **11**, and **10** (Table 1, entry 2) whilst 130 °C for 24 h in toluene delivers a 5:1 mixture of **12** and **11** only (Table 1, entry 5). Work up of this latter reaction afforded a 61% yield of **12**.

These results are open to interpretation in several ways involving two ambident anions **13** and **15** (Scheme 3). Thus competitive *O*- versus *C*-allylation would lead to mixture of **10** and **14** (not detected) and these, in turn might equilibrate via 3,3-sigmatropic shifts or regeneration of **13** by nucleophilic attack on the allyl moiety or reformation of the π-allylpalladium(II) species. We have carried out semi-empirical AM1 calculations on the 3,3-sigmatropic rearrangements of **10** ⇌ **14** and **11** ⇌ **12**. These data are shown in Scheme 4 and clearly indicate the greater stability of **14** versus **10** and **12** versus **11**. Deprotonation of **14** would generate ambident anion **15**, which could undergo competitive *O*- versus *C*-alkylation generating mixture of **11** and **12**. These latter compounds could then equilibrate via 3,3-sigmatropic shifts. Alternatively **10** could generate **11** directly by electrophilic attack of the π-allylpalladium species at C-4 (Scheme 3).

To probe the direct conversion of **10** to **11**, we subjected **10** (Ar=4-$MeOC_6H_4$) to a second cascade in toluene using methyl 4-iodobenzoate at 75 °C for 6 h and at 130 °C for 19 h. In both cases **10** (Ar=4-$MeOC_6H_4$) was recovered unchanged.[8] Thus **10** is not a precursor of **11**, **12** or **14** under these conditions.

These data are consistent with competitive O- and C-alkylation of **13** generating **10** and **14** with the latter undergoing rapid deprotonation to **15**, which, in turn, displays competitive O- and C-allylation generating mixture of **11** and **12**.

Further examples, carrying out the cascade at 130 °C in toluene for 24 h, employing different aryl iodides (2.4 mol equiv) with 10 mol % $Pd(OAc)_2$/20 mol % TFP and Cs_2CO_3 (2.0 mol equiv) afforded the expected *C*,*C*-diallylated

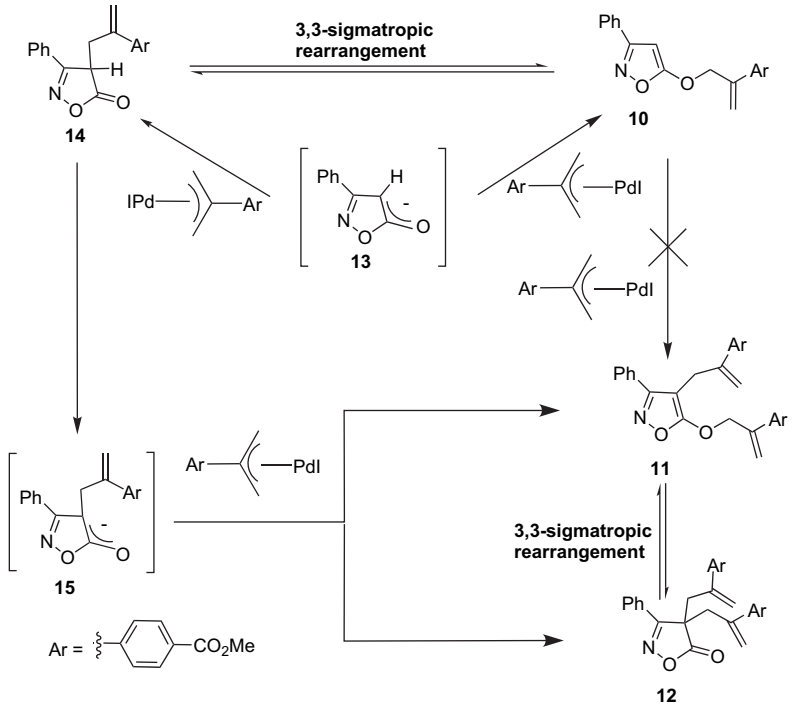


Scheme 2.

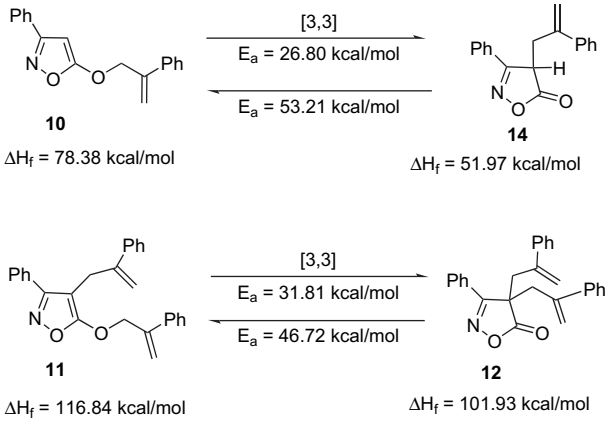
Table 1. Effect of the reaction conditions on product ratio from Scheme 2[a]

Entry	Catalyst	Base	Solvent	Temperature (°C)	Time (h)	Ratio[b] (**10/11/12**)
1	$Pd(OAc)_2$, PPh_3	Cs_2CO_3	Toluene	70	2	1:2:0
2	$Pd(OAc)_2$, PPh_3	Cs_2CO_3	Toluene	70	5	1:2:1
3	$Pd(OAc)_2$, TFP[c]	Cs_2CO_3	Toluene	50	5	1:2:0
4	$Pd(OAc)_2$, TFP[c]	Cs_2CO_3	Toluene	50	16	1:2:0
5[d]	$Pd(OAc)_2$, TFP[c]	Cs_2CO_3	Toluene	130	24	0:1:5
6	$Pd(OAc)_2$, TFP[c]	K_2CO_3	MeCN	50	5	0:2:1
7	$Pd(OAc)_2$, PPh_3	K_2CO_3	MeCN	50	5	0:4:1
8	$Pd(OAc)_2$, TFP[c]	K_2CO_3	MeCN	80	16	0:2:1
9	$Pd(OAc)_2$, PPh_3	K_2CO_3	DMF	40	5	1:0:0[e]
10	$Pd(PPh_3)_4$	K_2CO_3	DMF	40	16	1:0:0[e]
11	$Pd(OAc)_2$, PPh_3	K_2CO_3	DMF	40	24	1:0:0[e]

[a] Nucleophile (1.0 mmol), ArI (2.4 mmol), allene (1 atm), $Pd(OAc)_2$ (10 mol %) and PPh_3/TFP (20 mol %) and base (2.0 mmol).
[b] Ratio determined from the ^1H NMR of the crude product.
[c] Tris(2-furyl)phosphine.
[d] ArI (1.0 mmol) and nucleophile (1.5 equiv).
[e] Incomplete reaction.



Scheme 3.



Scheme 4.

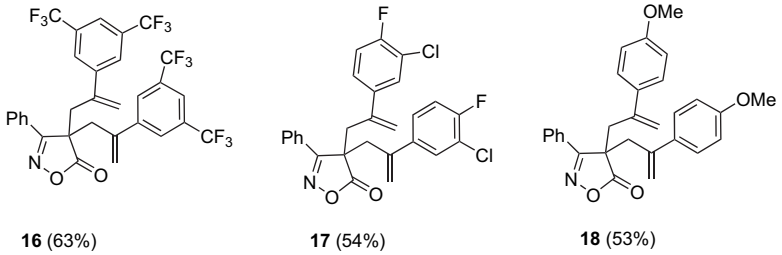
products **16**–**18**. Identical conditions, but for 20 h, were applied to 1-phenyl-3-methylpyrazolin-3-one **7** to afford **19**–**24** in 57–78% yield.

The effect of reaction temperature, time, solvent and base using **8a**[9] as nucleophile was also evaluated (Scheme 5, Table 2).

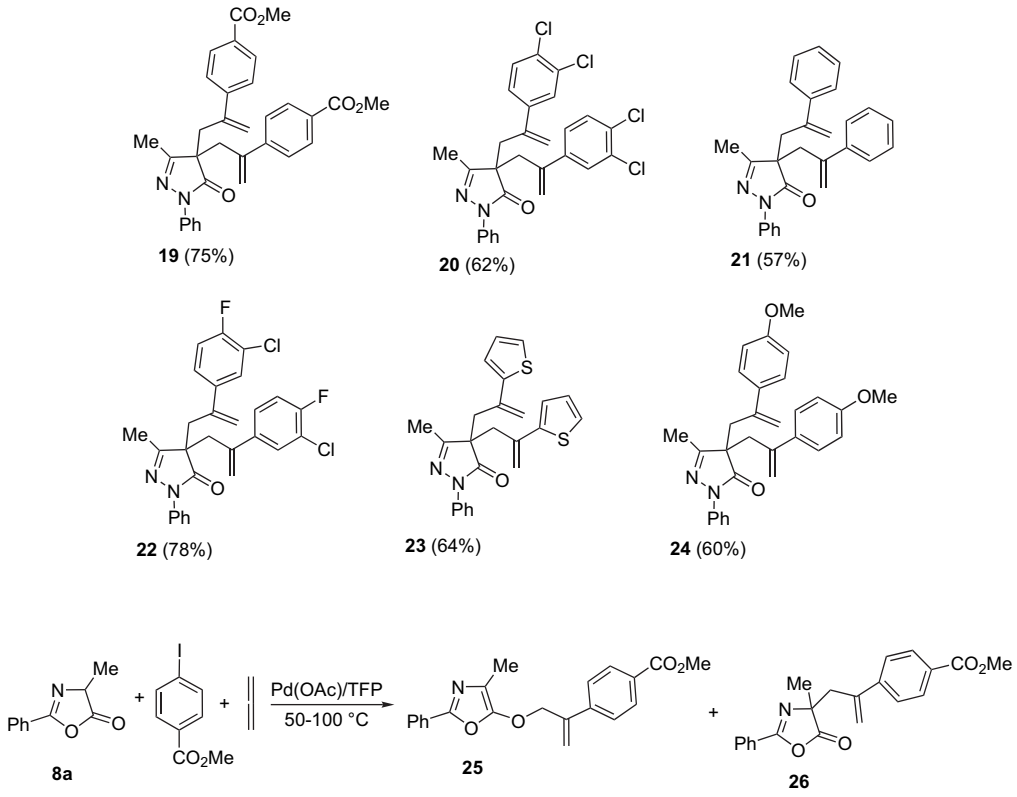
In MeCN the *C*-allylated product **26** increasingly predominates over the *O*-allylated product **25** as the temperature is raised from 50 to 100 °C (bath temperature). At 100 °C (Table 2, entry 6) **26** is the sole product. The implication of these results is that **25** regenerates either the π-allylpalladium(II) species or an equivalent allyl species allowing conversion to **26**, which bypasses the 3,3-sigmatropic route for this process. In toluene at 90 °C the reaction was non-selective (Table 2, entry 7). A series of aryl iodides were then utilized in the cascade using the conditions established in Table 2, entry 6. The expected products **26**–**29** were isolated in 55–72% yield.

Similar series, employing **8b**[9] and **8c**[9] as the nucleophiles, were carried out under the same conditions used for **8a** and afforded **30**–**33** in 54–91% yield and **34**–**37** in 49–61% yield.

N,*N*′-Dimethylbarbituric acid (**9**) proved to be an excellent substrate for the palladium catalyzed cascade (Scheme 6). The expected *C*,*C*-diallylated five-component cascade products **38**–**43** were obtained in high yield under slightly modified conditions with 5 mol % $Pd(PPh_3)_4$ as catalyst in MeCN at 80 °C (bath temperature) over 20 h.



16 (63%) **17** (54%) **18** (53%)

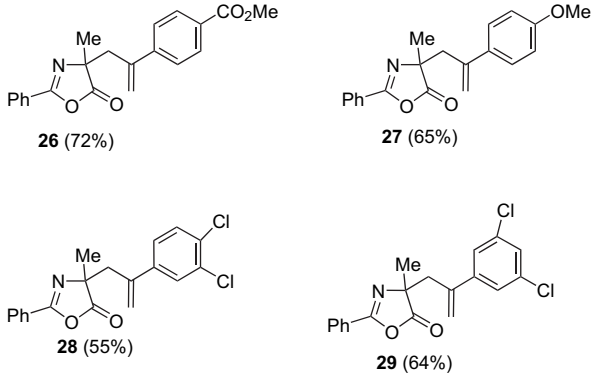


Scheme 5.

Table 2. Solvent and temperature effects on the ratio of **25** to **26**[a]

Entry	Catalyst	Base	Solvent	Temperature (°C)	Time (h)	Ratio[b] (**25**/**26**)
1	$Pd(OAc)_2$/TFP	K_2CO_3	MeCN	50	16	1:1
2	$Pd(OAc)_2$/TFP	K_2CO_3	MeCN	70	5	1:2
3	The crude residue from entry 2		MeCN	70	16	1:3
4	$Pd(OAc)_2$/TFP	K_2CO_3	MeCN	80	16	1:4
5	$Pd(OAc)_2$/TFP	K_2CO_3	MeCN	80	48	1:10
6	$Pd(OAc)_2$/TFP	K_2CO_3	MeCN	100	24	0:100
7	$Pd(OAc)_2$/TFP	Cs_2CO_3	Toluene	90	16	1:1

[a] ArI (1.0 mmol), nucleophile (1.5 mmol), allene (1 atm), $Pd(OAc)_2$ (10 mol %)/TFP (20 mol %) and base (2.0 mmol).
[b] Ratio determined from the ^1H NMR spectra of the crude product.



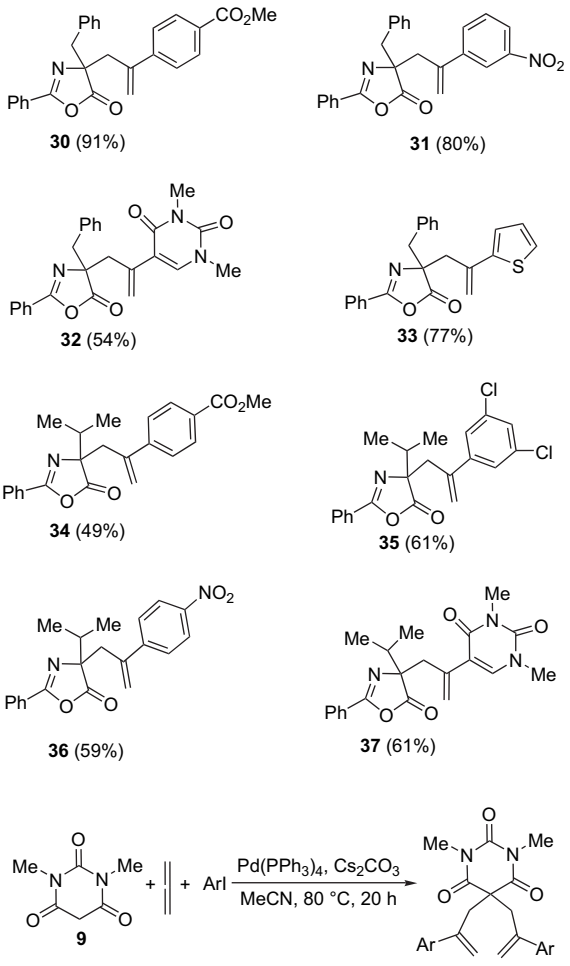
Several efforts were made to prepare the three-component mono-*C*-allylated product but in all cases diallylated product was obtained with only a trace (<10%) of monoallylated product. Cascade reactions using two different aryl iodides gave a mixture of all three possible five-component products (Scheme 7). The selectivity differed noticeably from that (1:2:1) expected statistically except in the case of entry 3 (Table 3). With the correct choice of aryl iodides such that the three products differed in polarity it proved easy to separate the mixtures.

The vinyl iodides 5-iodo-1,3-dimethyluracil and 5-iodo-1,3-dibenzyluracil were employed in five-component cascades (Scheme 8) furnishing the expected products **48** and **49** in excellent yield.

3. Experimental

3.1. General technical data

Melting points were determined on a Reichert hot-stage apparatus and are uncorrected. Infrared spectra were recorded on a Perkin–Elmer FTIR spectrometer either by a film



Scheme 6.

technique on sodium chloride discs by spreading a DCM solution of the compound on the disc and allowing it to evaporate or placing the solid in a Combi Pod attachment.

Microanalysis was obtained using a Carlo Erba MOD 1106 instrument. Mass spectra were recorded on a VG Autospec (EI) machine operating at 70 eV, a ZMD 2000 electrospray (ES) MS or a Quattro MS at the EPSRC service, Swansea. Accurate molecular weights were determined using perfluorokerosene as an internal standard.

Proton magnetic resonance spectra were recorded at 300 MHz on a Bruker DPX 300 instrument, at 250 MHz on a Bruker AC 250 instrument or at 500 MHz on a Bruker DRX 500 instrument. Chemical shifts are given in parts per million (δ) downfield from tetramethylsilane (δ 0.00) as an internal standard and coupling constants are given in hertz. The following abbreviations are used: s=singlet, d=doublet, t=triplet, q=quartet, dd=double doublet, m=multiplet, br s=broad singlet. ^{13}C NMR spectra were recorded at 75 MHz on a Bruker DPX 300 instrument and chemical shift values are reported in parts per million (ppm) relative to $CDCl_3$ (δ=77.0). Deuteriochloroform was used as the solvent unless otherwise stated.

Flash column chromatography was performed on silica gel 60 (230–400 mesh). R_f values were determined by thin layer chromatography (TLC) on Merck silica 60 F_{254} and spots were visualized by UV light and/or by developing with $KMnO_4$ solution.

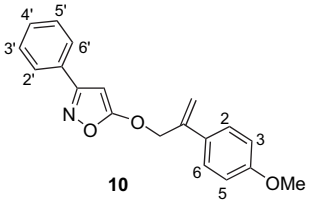
All compounds were named using the ACD/ILAB web service (http://www.acdlabs.com), according to the IUPAC system.

The term ether refers to diethyl ether and petroleum ether refers to the fraction with boiling point 40–60 °C. Commercially available reagents were used as purchased.

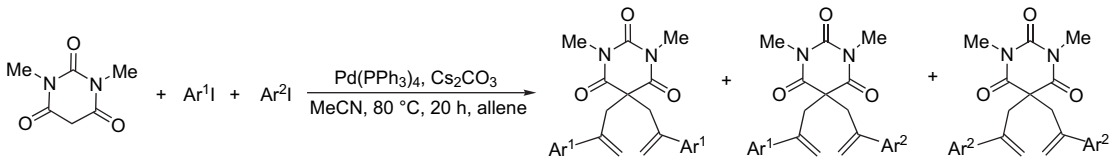
3.2. General procedure (A) for 3-phenyl-5-isoxazolone (6) as a nucleophile

A mixture of nucleophile (1.0 mmol), aryl or heteroaryl iodide (2.4 mmol), $Pd(OAc)_2$ (10 mol %), tris(2-furyl)phosphine (20 mol %) and Cs_2CO_3 (2.0 mol equiv) in toluene (20 ml) was stirred for 15 min in Schlenk tube. Then the mixture was subjected to two freeze, pump, thaw cycles and charged with allene gas (1 bar). After warming to room temperature, the mixture was stirred at 130 °C in an oil bath for another 25 h, cooled to room temperature, excess allene was vented and the solvent was evaporated. The residue was purified by column chromatography on silica gel.

3.2.1. 5-{[2-(4-Methoxyphenyl)prop-2-en-1-yl]oxy}-3-phenylisoxazole (10).

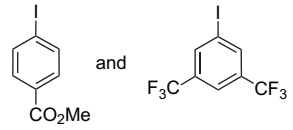
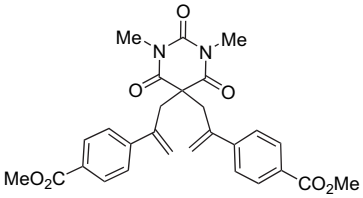
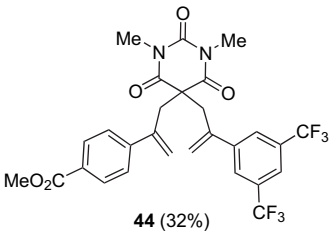
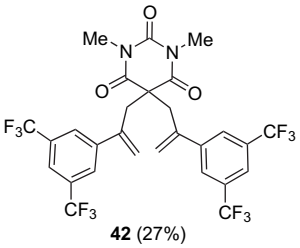
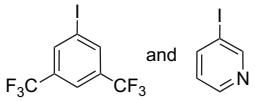
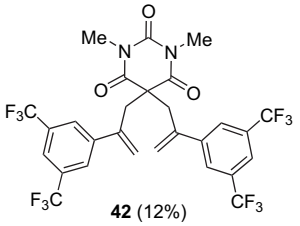
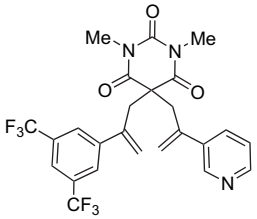
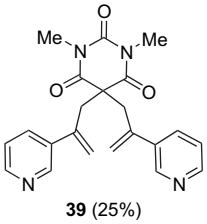
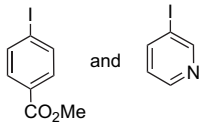
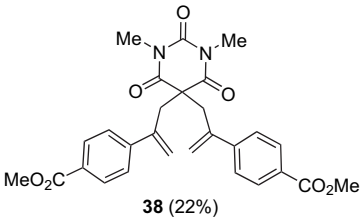
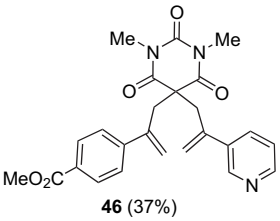
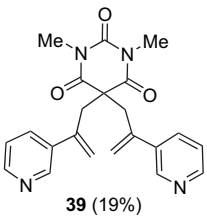
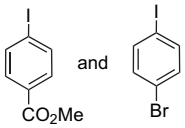
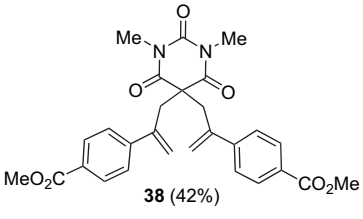
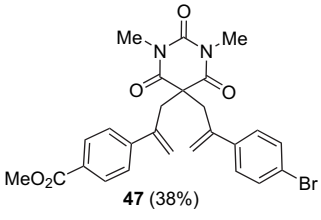
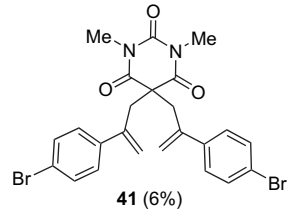


Prepared from 3-phenyl-5-isoxazolone and methyl 4-iodobenzoate by general procedure A at 50 °C for 16 h. Column chromatography eluting with 1:1 v/v hexane–Et_2O (R_f 0.05)

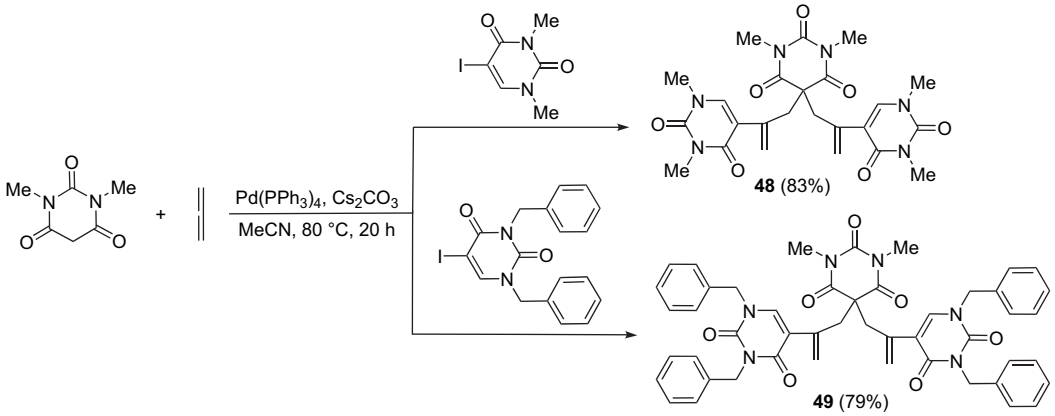


Scheme 7.

Table 3. Products from Scheme 6[a,b]

Entry	Aryl iodides	Product **1**	Product **2**	Product **3**
1		 **38** (31%)	 **44** (32%)	 **42** (27%)
2		 **42** (12%)	 **45** (21%)	 **39** (25%)
3		 **38** (22%)	 **46** (37%)	 **39** (19%)
4		 **38** (42%)	 **47** (38%)	 **41** (6%)

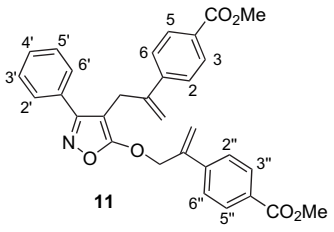
[a] *N*,*N*′-Dimethylbarbituric acid (1.0 mmol), Ar^1I (1.2 equiv), Ar^2I (1.2 equiv), allene (1 atm) and base (2.0 mol equiv) in MeCN at 80 °C for 20 h.
[b] Isolated yields.



Scheme 8. *N*,*N*′-Dimethylbarbituric acid (1.0 mmol), ArI (2.4 equiv), Cs_2CO_3 (2.0 mol equiv), $Pd(PPh_3)_4$ (5 mol %), MeCN (20 ml), 80 °C, 20 h.

afforded **10** (17%) as a colourless viscous oil. (Found: C, 74.05; H, 5.60; N, 4.30. $C_{19}H_{17}NO_3$ requires: C, 74.25; H, 5.50; N, 4.55%.) δ_H (500 MHz, $CDCl_3$) 3.80 (3H, s, OMe), 4.50 (2H, s, OCH_2), 5.35 (1H, s, 4-isoxazolone–H), 5.31 and 5.41 (2×1H, 2×s, $=CH_2$), 6.78 (2H, d, *J* 8.7 Hz, 3-H and 5-H), 7.13 (2H, d, *J* 8.7 Hz, 2-H and 6-H), 7.35 (2H, d, *J* 7.9 Hz, 2′-H and 6′-H), 7.45 (2H, dd *J* 7.9 and 7.2 Hz, 3′-H and 5′-H) and 7.52 (1H, m, 4′-H); δ_C (75 MHz, $CDCl_3$) 55.7, 57.3, 91.7, 113.9, 116.8, 127.5, 129.6, 131.3, 131.9, 140.9, 159.9 and 169.2; *m*/*z* % (ES) 308 (M^++H, 100); ν_{max}/cm^{-1} (film) 3060, 2980 and 1680.

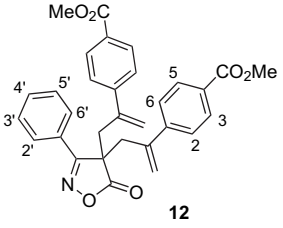
3.2.2. Methyl 4-(1-{[5-({2-[4-(methoxycarbonyl)phenyl]-prop-2-en-1-yl}oxy)-3-phenylisoxazol-4-yl]methyl}vinyl)benzoate (11).



11

Prepared from 3-phenyl-5-isoxazolone and methyl 4-iodobenzoate by general procedure A at 100 °C for 16 h. Column chromatography eluting with 1:1 v/v hexane–ethyl acetate (R_f 0.25) afforded **11** (55%) as colourless needles, mp 130–132 °C. (Found: C, 72.95; H, 5.30; N, 2.85. $C_{31}H_{27}NO_6$ requires: C, 73.05; H, 5.30; N, 2.75%.) δ_H (500 MHz, $CDCl_3$) 3.39 (2H, s, CCH_2), 3.90 and 3.92 (2×3H, 2×s, 2×OMe), 4.40 (2H, s, OCH_2), 4.98, 5.40, 5.42 and 5.53 (4×1H, 4×s, 2×$=CH_2$), 7.20 (2H, d, *J* 7.3 Hz, 2′-H and 6′-H), 7.22 (2H, d, *J* 8.1 Hz, 2″-H and 6″-H), 7.34 (2H, d, *J* 8.1 Hz, 2-H and 6-H), 7.42 (2H, dd, *J* 7.7 and 7.3 Hz, 3′-H and 5′-H), 7.50–7.52 (1H, m, 4′-H), 7.91 and 7.92 (2×2H, 2×d, *J* 8.1 Hz, 3-H, 5-H, 3″-H and 5″-H); δ_C (75 MHz, $CDCl_3$) 28.4, 52.4, 57.2, 117.2, 120.7, 126.4, 126.8, 128.5, 129.6, 129.9, 130.1, 131.6, 142.2, 144.9 and 179.6 (CO); *m*/*z* % (ES) 527 (M+NH_4^+, 100); ν_{max}/cm^{-1} (film) 3054, 2987, 1742 and 1632.

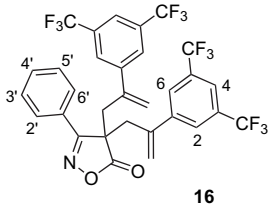
3.2.3. Dimethyl 4,4′-[(5-oxo-3-phenyl-4,5-dihydroisoxazole-4,4-diyl)diprop-1-ene-3,2-diyl]dibenzoate (12).



12

Prepared from 3-phenyl-5-isoxazolone and methyl 4-iodobenzoate by general procedure A. Column chromatography eluting with 1:1 v/v hexane–ethyl acetate (R_f 0.35) afforded **12** (61%) as a colourless solid, which crystallized from hexane–ethyl acetate as colourless plates, mp 105–107 °C. (Found: C, 72.90; H, 5.10; N, 2.60. $C_{31}H_{27}NO_6$ requires: C, 73.05; H, 5.30; N, 2.75%.) δ_H (500 MHz, $CDCl_3$) 3.29 and 3.30 (2×2H, 2×d, *J* 14.2 Hz, 2×CH_2), 3.86 (6H, s, 2×OMe), 5.11 and 5.18 (2×2H, 2×s, 2×$=CH_2$), 7.09 (4H, d, *J* 8.1 Hz, 2×2-H and 2×6-H), 7.11–7.14 (2H, m, 3′-H and 5′-H), 7.28 (1H, m, 4′-H), 7.32 (2H, d, *J* 7.7 Hz, 2′-H and 6′-H) and 7.71 (4H, d, *J* 8.1 Hz, 2×3-H and 2×5-H); δ_C (75 MHz, $CDCl_3$) 42.3 (CH_2), 52.4 (OMe), 57.2, 120.9 ($=CH_2$), 126.5, 127.2, 128.3, 128.8, 129.6, 131.6, 142.2, 144.9, 167.0 (CO) and 179.6 (CO); *m*/*z* % (ES) 510 (M^++H, 85); ν_{max}/cm^{-1} (film) 3054, 2988, 1793 and 1634.

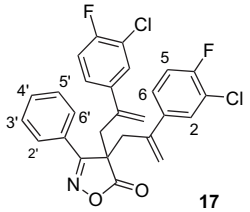
3.2.4. 4,4-Bis{2-[3,5-bis(trifluoromethyl)phenyl]prop-2-en-1-yl}-3-phenylisoxazol-5(4*H*)-one (16).



16

Prepared from 3-phenyl-5-isoxazolone and 3,5-bis(trifluoromethyl)iodobenzene by general procedure A. Column chromatography eluting with 4:1 v/v hexane–Et_2O (R_f 0.06) afforded **16** (63%) as colourless plates, mp 55–57 °C. (Found: C, 55.95; H, 2.90; N, 1.90. $C_{31}F_{12}H_{19}NO_2$ requires: C, 55.95; H, 2.85; N, 2.10%.) δ_H (500 MHz, $CDCl_3$) 3.33 and 3.31 (2×2H, 2×d, *J* 13.9 Hz, 2×CH_2), 5.25 and 5.32 (2×2H, 2×s, 2×$=CH_2$), 7.00–7.04 (2H, dd, *J* 8.1 and 7.7 Hz, 3′-H and 5′-H), 7.16–7.19 (3H, m, 2′-H, 6′-H and 4′-H), 7.40 (4H, s, 2×2-H and 2×6-H) and 7.46 (2H, s, 2×4-H); δ_C (75 MHz, $CDCl_3$) 41.9, 57.6, 117.4, 121.0, 121.4, 125.3, 126.0, 127.1, 128.3, 128.5, 128.9, 131.9 (q, J_{C-F} 33.3 Hz, *C*–CF_3), 140.4, 142.2, 164.6 and 179.0 (CO); *m*/*z* % (ES) 666 (M^++H, 40); ν_{max}/cm^{-1} (film) 3054, 2987, 1795 and 1265.

3.2.5. 4,4-Bis[2-(3-chloro-4-fluorophenyl)prop-2-en-1-yl]-3-phenylisoxazol-5(4*H*)-one (17).

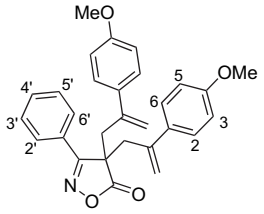


17

Prepared from 3-phenyl-5-isoxazolone and 3-chloro-4-fluoroiodobenzene by general procedure A. Column chromatography eluting with 4:1 v/v hexane–Et_2O (R_f 0.1) afforded **17** (54%) as colourless plates, mp 34–36 °C. (Found: C, 65.25; H, 3.80; Cl, 14.10; N, 2.75. $C_{27}Cl_2F_2H_{19}NO_2$ requires: C, 65.05; H, 3.80; Cl, 14.25; N, 2.80%.) δ_H (500 MHz, C_6D_6) 2.58 and 2.80 (2×2H, 2×d, *J* 14.0 Hz, 2×CH_2), 4.80 and 5.06 (2×2H, 2×s, 2×$=CH_2$), 6.33 (2H, dd, J_{H-F} 8.9 and 8.5 Hz, 2×5-H), 6.47 (2H, ddd, *J* 8.5, J_{H-F} 6.8 and 2.1 Hz, 2×6-H), 6.76 (2H, dd, *J* 8.1 and 7.6 Hz, 3′-H and 5′-H), 6.80 (1H, m, 4′-H), 6.81 (2H, dd, J_{H-F} 6.8 and 2.1 Hz, 2×2-H) and 7.00 (2H, d, *J* 8.1 Hz, 2′-H and 6′-H); δ_C (75 MHz, $CDCl_3$) 42.7 (CH_2), 57.5, 116.5, 120.8 ($=CH_2$), 126.2, 127.7, 128.1, 128.8, 129.6, 131.9, 137.4, 141.0, 165.5 and 179.6 (CO); *m*/*z* % (ES) 501

(M^+, 2×^{37}Cl, 11), 499 (M^+, ^{37}Cl and ^{35}Cl, 66) and 497 (M^+, 2×^{35}Cl, 100); ν_{max}/cm^{-1} (film) 3055, 2987, 1794 and 1631.

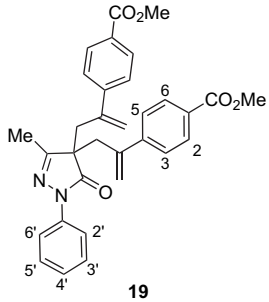
3.2.6. 4,4-Bis[2-(4-methoxyphenyl)prop-2-en-1-yl]-3-phenylisoxazol-5(4*H*)-one (18).



18

Prepared from 3-phenyl-5-isoxazolone and 4-iodoanisole by general procedure A. Column chromatography eluting with 1:1 v/v hexane–Et_2O (R_f 0.25) afforded **18** (53%) as colourless plates, mp 78–80 °C. (Found: C, 76.65; H, 5.70; N, 2.80. $C_{29}H_{27}NO_4$ requires: C, 76.80; H, 5.95; N, 3.05%.) δ_H (500 MHz, $CDCl_3$) 3.24 (4H, s, 2×CH_2), 3.70 (6H, s, 2×OMe), 4.92 and 5.02 (2×2H, 2×s, 2×=CH_2), 6.58 (4H, d, *J* 8.5 Hz, 2×3-H and 2×5-H), 6.97 (4H, d, *J* 8.5 Hz, 2×2-H and 2×6-H), 7.21 (2H, dd, *J* 8.1 and 7.2 Hz, 3′-H and 5′-H), 7.30–7.32 (1H, m, 4′-H) and 7.40 (2H, d, *J* 8.1 Hz, 2′-H and 6′-H); δ_C (75 MHz, $CDCl_3$) 43.1 (CH_2), 55.5 (Me), 57.1, 113.6, 117.9 (=CH_2), 126.8, 128.5, 128.6, 128.9, 131.1, 132.7, 142.6, 159.6, 166.0 and 180.0 (CO); *m/z* % (ES) 454 (M^++H, 100); ν_{max}/cm^{-1} (film) 3054, 2987, 1793 and 1666.

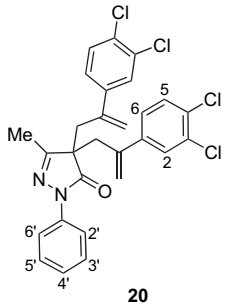
3.2.7. Dimethyl 4,4′-[(3-methyl-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazole-4,4-diyl)diprop-1-ene-3,2-diyl]dibenzoate (19).



19

Prepared from 3-methyl-1-phenyl-2-pyrazolin-5-one and methyl 4-iodobenzoate by general procedure A. Column chromatography eluting with 2:3 v/v petroleum ether–Et_2O (R_f 0.16) afforded **19** (75%) as a colourless solid, which crystallized from petroleum ether–Et_2O as colourless rods, mp 113–114 °C. (Found: C, 73.40; H, 5.70; N, 5.35. $C_{32}H_{30}N_2O_5$ requires: C, 73.55; H, 5.80; N, 5.35%.) δ_H (300 MHz, $CDCl_3$) 1.56 (3H, s, Me), 2.82 and 3.19 (2×2H, 2×d, *J* 13.9 Hz, 2×CH_2), 3.84 (6H, s, 2×OMe), 5.12 and 5.15 (2×2H, 2×s, 2×=CH_2), 7.05 (1H, t, *J* 7.3 Hz, 4′-H), 7.18–7.22 (6H, m, 3′-H, 5′-H, 2×3-H and 2×5-H), 7.32 (2H, d, *J* 7.8 Hz, 2′-H and 6′-H) and 7.81 (4H, d, *J* 8.2 Hz, 2×2-H and 2×6-H); δ_C (75 MHz, $CDCl_3$) 15.1 (Me), 41.5 (CH_2), 52.4 (Me), 60.3, 118.9, 119.6 (=CH_2), 125.1, 127.3, 128.7, 129.6, 129.8, 137.6, 143.6, 145.6, 161.4, 167.0 (CO) and 173.7 (CO); *m/z* % (ES) 523 (M^++H, 100); ν_{max}/cm^{-1} (film) 3420, 3031, 2998, 2952, 2928, 2852, 1939, 1722, 1625 and 1608.

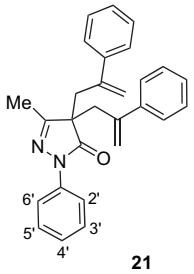
3.2.8. 4,4-Bis[(3,4-dichlorophenyl)prop-2-en-1-yl]-5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one (20).



20

Prepared from 3-methyl-1-phenyl-2-pyrazolin-5-one and 3,4-dichloroiodobenzene by general procedure A. Column chromatography eluting with 1:1 v/v petroleum ether–Et_2O (R_f 0.24) afforded **20** (62%) as a pale brown oil. (Found: C, 61.70; H, 3.90; N, 5.05; Cl, 26.35. $C_{28}H_{22}Cl_4N_2O$ requires: C, 61.80; H, 4.05; N, 5.15; Cl, 26.05%.) δ_H (300 MHz, $CDCl_3$) 1.74 (3H, s, Me), 2.72 and 3.13 (2×2H, 2×d, *J* 14.0 Hz, 2×CH_2), 5.04 and 5.10 (2×2H, 2×s, 2×=CH_2), 6.95 (2H, dd, *J* 8.2 and 1.4 Hz, 2×6-H), 7.10 (1H, m, 4′-H), 7.17 (2H, d, *J* 1.4 Hz, 2×2-H) and 7.20–7.32 (6H, m, 2′-H, 3′-H, 5′-H, 6′-H and 2×5-H); δ_C (75 MHz, $CDCl_3$) 15.3 (Me), 41.6 (CH_2), 60.0, 118.6, 119.6 (=CH_2), 125.4, 126.8, 128.9, 129.2, 130.3, 132.1, 132.5, 137.4, 140.7, 142.4, 161.3 (CO) and 173.7 (CO); *m/z* % (ES) 545 (M^++H, ^{37}Cl and 3×^{35}Cl, 100); ν_{max}/cm^{-1} (film) 3672, 3414, 3083, 3063, 2985, 2922, 2849, 1758, 1708 and 1627.

3.2.9. 5-Methyl-2-phenyl-4,4-bis(2-phenylprop-2-en-1-yl)-2,4-dihydro-3*H*-pyrazol-3-one (21).

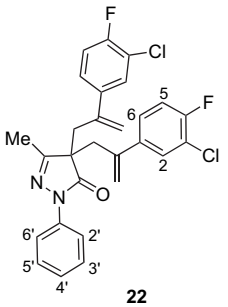


21

Prepared from 3-methyl-1-phenyl-2-pyrazolin-5-one and iodobenzene by general procedure A. Column chromatography eluting with 4:1 v/v petroleum ether–Et_2O (R_f 0.23) afforded **21** (57%) as a colourless solid, which crystallized from petroleum ether–Et_2O as colourless prisms, mp 71–73 °C. (Found: C, 82.50; H, 6.50; N, 7.05. $C_{28}H_{26}N_2O$ requires: C, 82.70; H, 6.45; N, 6.90%.) δ_H (300 MHz, $CDCl_3$) 1.47 (3H, s, Me), 2.78 and 3.16 (2×2H, 2×d, *J* 13.8 Hz, 2×CH_2), 5.03 and 5.06 (2×2H, 2×s, 2×=CH_2), 7.04–7.13 (11H, m, 2×Ph and 4′-H), 7.23 (2H, t, *J* 8.0 Hz, 3′-H and 5′-H) and 7.36 (2H, d, *J* 8.0 Hz, 2′-H and 6′-H); δ_C (75 MHz, $CDCl_3$) 15.0 (Me), 30.1, 42.0 (CH_2), 60.6, 118.1, 119.5 (=CH_2), 125.2, 127.4, 128.1, 128.5, 128.8, 138.0, 141.4, 144.4, 161.9 (CO) and 174.1 (CO); *m/z* (ES) (%) 407 (M^++H, 100); ν_{max}/cm^{-1} (film) 3699, 3389, 3081,

3034, 2983, 2942, 2911, 1951, 1878, 1818, 1763 and 1702 (CO).

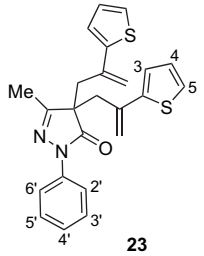
3.2.10. 4,4-Bis[(3-chloro-4-fluorophenyl)prop-2-en-1-yl]-5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one (22).



22

Prepared from 3-methyl-1-phenyl-2-pyrazolin-5-one and 3-chloro-4-fluoroiodobenzene by general procedure A. Column chromatography eluting with 7:3 v/v petroleum ether–Et_2O (R_f 0.15) afforded **22** (78%) as a pale brown oil. (Found: C, 65.85; H, 4.65; N, 5.50; Cl, 13.95. $C_{28}H_{22}Cl_2F_2N_2O$ requires: C, 65.75; H, 4.35; N, 5.45; Cl, 13.85%.) δ_H (500 MHz, $CDCl_3$) 1.47 (3H, s, Me), 2.74 and 3.13 (2×2H, 2×d, J 14.0 Hz, 2×CH_2), 5.02 and 5.09 (2×2H, 2×s, 2×=CH_2), 6.85 (2H, t, J 8.7 Hz, 2×5-H, where $J_{H-H}\sim J_{H-F}$), 6.96–6.99 (2H, m, 2×6-H), 7.07 (1H, t, J 7.3 Hz, 4′-H), 7.14–7.16 (2H, dd, J 6.9 and 1.9 Hz, 2×2-H), 7.24 (2H, t, J 7.9 Hz, 3′-H and 5′-H) and 7.35 (2H, d J 8.1 Hz, 2′-H and 6′-H); δ_C (75 MHz, $CDCl_3$) 15.2 (Me), 41.9 (CH_2), 60.0, 116.3, 116.6, 118.6, 119.2 (=CH_2), 120.8, 121.1, 125.3, 127.2, 127.3, 128.8, 129.5, 137.8, 137.9, 142.4, 156.3, 159.6, 161.4 (CO) and 173.7 (CO); *m/z* % (ES) 415 (M^+, 2×^{37}Cl, 11), 413 (M^+, ^{37}Cl and ^{35}Cl, 66) and 411 (M^+, 2×^{35}Cl, 100); ν_{max}/cm^{-1} (film) 3407, 3064, 2922, 1708 and 1628.

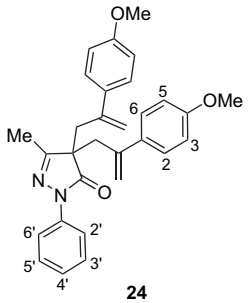
3.2.11. 5-Methyl-2-phenyl-4,4-bis[2-(2-thienyl)prop-2-en-1-yl]-2,4-dihydro-3*H*-pyrazol-3-one (23).



23

Prepared from 3-methyl-1-phenyl-2-pyrazolin-5-one and 2-iodothiophene by general procedure A. Column chromatography eluting with 9:1 v/v petroleum ether–Et_2O (R_f 0.13) afforded **23** (64%) as a colourless oil. (Found: C, 68.75; H, 5.30; N, 6.75; S, 15.25. $C_{24}H_{22}N_2OS_2$ requires: C, 68.85; H, 5.30; N, 6.70; S, 15.30%.) δ_H (500 MHz, $CDCl_3$) 1.77 (3H, s, Me), 2.82 and 3.15 (2×2H, 2×d, J 14.3 Hz, 2×CH_2), 4.94 and 5.28 (2×2H, 2×s, 2×=CH_2), 6.85 (2H, dd, J 5.1 and 3.6 Hz, 2×4-H), 6.95 (2H, d, J 3.6 Hz, 2×3-H), 7.06 (2H, d, J 5.1 Hz, 2×5-H), 7.11 (1H, t, J 7.3 Hz, 4′-H), 7.26–7.30 (2H, t, J 7.8 Hz, 3′-H and 5′-H) and 7.54 (2H, d, J 8.0 Hz, 2′-H and 6′-H); δ_C (75 MHz, $CDCl_3$) 15.3 (Me), 41.6 (CH_2), 60.1, 116.3, 119.7 (=CH_2), 125.0, 125.3, 125.5, 127.7, 129.0, 136.7, 138.0, 144.5, 161.9 (CO) and 174.5 (CO); *m/z* % (ES) 419 (M^++H, 100); ν_{max}/cm^{-1} (film) 3839, 3540, 3380, 3070, 3032, 1708 and 1614.

3.2.12. 4,4-Bis[(4-methoxyphenyl)prop-2-en-1-yl]-5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one (24).



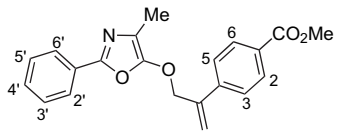
24

Prepared from 3-methyl-1-phenyl-2-pyrazolin-5-one and 4-iodoanisole by general procedure A. Column chromatography eluting with 7:3 v/v petroleum ether–Et_2O (R_f 0.13) afforded **24** (60%) as a colourless oil. (Found: C, 77.0; H, 6.25; N, 5.95. $C_{30}H_{30}N_2O$ requires: C, 77.25; H, 6.50; N, 6.00%.) δ_H (300 MHz, $CDCl_3$) 1.58 (3H, s, Me), 2.74 and 3.15 (2×2H, 2×d, J 13.8 Hz, 2×CH_2), 3.62 (6H, s, 2×OMe), 4.97 and 4.99 (2×2H, 2×s, 2×=CH_2), 6.64 (4H, d, J 8.6 Hz, 2×3-H and 2×5-H), 7.06 (5H, m, 2×2-H, 2×6-H and 4′-H), 7.19–7.24 (2H, m, 3′-H and 5′-H) and 7.33 (2H, d, J 7.4 Hz, 2′-H and 6′-H); δ_C (75 MHz, $CDCl_3$) 15.2 (Me), 42.3, 55.6, 60.4, 113.7, 116.7, 119.3 (=CH_2), 125.0, 128.5, 128.6, 133.5, 138.0, 144.0, 159.6, 162.0 and 174.3 (CO); *m/z* % (ES) 467 (M^++H, 100); ν_{max}/cm^{-1} (film) 3035, 3001, 2953, 2934, 2836, 1709 and 1606.

3.3. General procedure (B) for the three-component cascade using 4-methyl-2-phenyl-4*H*-oxazol-5-one (8a) as pronucleophile

Identical to procedure A except that a mixture of aryl iodide (1.0 mmol, 1.0 mol equiv), nucleophile (1.5 mmol, 1.5 mol equiv) and K_2CO_3 (2.0 mol equiv) in MeCN (20 ml) was heated at 100 °C for 24 h.

3.3.1. Methyl 4-(1-{[(4-methyl-2-phenyl-1,3-oxazol-5-yl)oxy]methyl}vinyl)benzoate (25).

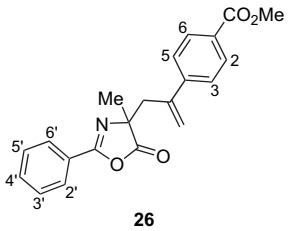


25

Prepared from methyl 4-iodobenzoate and 4-methyl-2-phenyl-4*H*-oxazol-5-one by general procedure B at 50 °C for 16 h. Column chromatography eluting with 4:1 v/v hexane–Et_2O (R_f 0.2) afforded **25** (48%) as a pale yellow oil. (Found: C, 72.00; H, 5.65; N, 4.05. $C_{21}H_{19}NO_4$ requires: C, 72.20; H, 5.40; N, 4.00%.) δ_H (300 MHz, $CDCl_3$) 2.16 (3H, s, Me), 3.91 (3H, s, OMe), 4.85 (2H, s, OCH_2), 5.24 and 5.45 (2×1H, 2×s, =CH_2), 7.37 (2H, d, J 8.4 Hz, 3-H and 5-H), 7.39–7.42 (2H, m, 3′-H and 5′-H), 7.46–7.55

(3H, m, 2′-H, 4′-H and 6′-H) and 7.96 (2H, d, *J* 8.4 Hz, 2-H and 6-H); δ_C (75 MHz, $CDCl_3$) 26.7 (Me), 49.2, 52.5, 116.1 (CH_2), 126.8, 128.6, 129.2, 130.1, 132.9, 143.7, 143.9 and 167.1; *m/z* % (ES) 349 (M^+, 100); ν_{max}/cm^{-1} (film) 3049, 2985 and 1655.

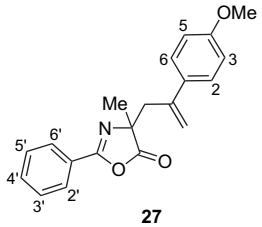
3.3.2. Methyl 4-{1-[(4-methyl-5-oxo-2-phenyl-4,5-dihydro-1,3-oxazol-4-yl)methyl]vinyl}benzoate (26).



26

Prepared from methyl 4-iodobenzoate and 4-methyl-2-phenyl-4*H*-oxazol-5-one by general procedure B. Column chromatography eluting with 4:1 v/v hexane–Et_2O (R_f 0.25) afforded **26** (72%) as a colourless solid, which crystallized form ether as colourless needles, mp 68–70 °C. (Found: C, 71.95; H, 5.40; N, 3.90. $C_{21}H_{19}NO_4$ requires: C, 72.20; H, 5.40; N, 4.00%.) δ_H (500 MHz, $CDCl_3$) 1.57 (3H, s, Me), 3.08 and 3.21 (2×1H, 2×d, *J* 13.8 Hz, CH_2), 3.88 (3H, s, OMe), 5.28 and 5.36 (2×1H, 2×s, =CH_2), 7.31 (2H, d, *J* 8.0 Hz, 3-H and 5-H), 7.34–7.36 (2H, m, 3′-H and 5′-H), 7.48 (1H, m, 4′-H), 7.60 (2H, d, *J* 7.9 Hz, 2′-H and 6′-H) and 7.82 (2H, d, *J* 8.0 Hz, 2-H and 6-H); δ_C (75 MHz, $CDCl_3$) 24.4 (Me), 44.0 (CH_2), 52.4 (Me), 71.0, 120.1 (=CH_2), 125.8, 126.9, 128.1, 128.9, 129.3, 129.8, 133.0, 143.2, 145.9, 160.1, 167.2 and 180.4; *m/z* % (ES) 350 ($M+H^+$, 100); ν_{max}/cm^{-1} (film) 3054, 2987, 1817, 1718, 1656 and 1608.

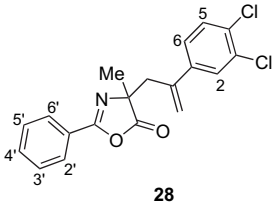
3.3.3. 4-[2-(4-Methoxyphenyl)prop-2-en-1-yl]-4-methyl-2-phenyl-1,3-oxazol-5(4*H*)-one (27).



27

Prepared from methyl 4-iodoanisole and 4-methyl-2-phenyl-4*H*-oxazol-5-one by general procedure B. Column chromatography eluting with 9:1 v/v hexane–Et_2O (R_f 0.1) afforded **27** (65%) as a colourless solid, which crystallized from ether as colourless needles, mp 38–40 °C. (Found: C, 75.00; H, 5.90; N, 4.20. $C_{20}H_{19}NO_3$ requires: C, 74.75; H, 5.90; N, 4.35%.) δ_H (500 MHz, $CDCl_3$) 1.56 (3H, s, Me), 3.04 and 3.15 (2×1H, 2×d, *J* 13.8 Hz, CH_2), 3.71 (3H, s, OMe), 5.10 and 5.20 (2×1H, 2×s, =CH_2), 6.68 (2H, d, *J* 8.6 Hz, 3-H and 5-H), 7.18 (2H, d, *J* 8.6 Hz, 2-H and 6-H), 7.35–7.38 (2H, m, 3′-H and 5′-H′), 7.49 (1H, m, 4′-H) and 7.66 (2H, d, *J* 7.9 Hz, 2′-H and 6′-H); δ_C (75 MHz, $CDCl_3$) 24.5 (Me), 44.3 (CH_2), 55.6 (OMe), 70.9, 113.8, 116.9 (=CH_2), 126.1, 128.1, 128.8, 132.8, 133.7, 143.2, 159.4 and 180.7 (CO); *m/z* % (ES) 322 (M^++H, 100); ν_{max}/cm^{-1} (film) 3054, 2985, 1817 and 1656.

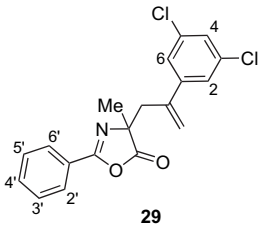
3.3.4. 4-[2-(3,4-Dichlorophenyl)prop-2-en-1-yl]-4-methyl-2-phenyl-1,3-oxazol-5(4*H*)-one (28).



28

Prepared from 3,4-dichloroiodobenzene and 4-methyl-2-phenyl-4*H*-oxazol-5-one by general procedure B. Column chromatography eluting with 9:1 v/v hexane–Et_2O (R_f 0.15) afforded **28** (55%) as colourless plates, mp 48–50 °C. (Found: C, 63.60; H, 4.00; N, 3.70; Cl, 19.50. $C_{19}H_{15}Cl_2NO_2$ requires: C, 63.35; H, 4.20; N, 3.85; Cl, 19.70%.) δ_H (500 MHz, $CDCl_3$) 1.57 (3H, s, Me), 3.01 and 3.13 (2×1H, 2×d, *J* 13.8 Hz, CH_2), 5.23 and 5.29 (2×1H, 2×s, =CH_2), 7.08 (1H, dd, *J* 8.2 and 1.7 Hz, 6-H), 7.21 (1H, d, *J* 8.2 Hz, 5-H), 7.31 (1H, d, *J* 1.7 Hz, 2-H), 7.39 (2H, dd, *J* 8.1 and 7.2 Hz, 3′-H and 5′-H), 7.50–7.53 (1H, m, 4′-H) and 7.65 (2H, d, *J* 8.1 Hz, 2′-H and 6′-H); δ_C (75 MHz, $CDCl_3$) 24.3 (Me), 44.0 (CH_2), 71.0, 119.9 (=CH_2), 125.6, 126.3, 128.0, 129.0, 129.1, 130.2, 133.1, 141.4, 143.4, 160.3 and 180.2 (CO); *m/z* % (ES) 360 (M^++H, 2×^{35}Cl, 100); ν_{max}/cm^{-1} (film) 2932, 1818 and 1655.

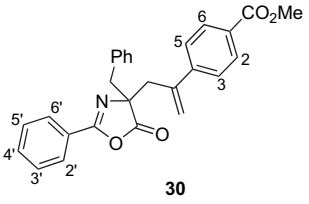
3.3.5. 4-[2-(3,5-Dichlorophenyl)prop-2-en-1-yl]-4-methyl-2-phenyl-1,3-oxazol-5(4*H*)-one (29).



29

Prepared from 3,5-dichloroiodobenzene and 4-methyl-2-phenyl-4*H*-oxazol-5-one by general procedure B. Column chromatography eluting with hexane (R_f 0.1) afforded **29** (64%) as a pale yellow oil. (Found: C, 63.25; H, 4.00; N, 3.90; Cl, 19.70. $C_{19}H_{15}Cl_2NO_2$ requires: C, 63.35; H, 4.20; N, 3.85 Cl, 19.70%.) δ_H (500 MHz, $CDCl_3$) 1.57 (3H, s, Me), 3.00 and 3.11 (2×1H, 2×d, *J* 13.9 Hz, CH_2), 5.26 and 5.30 (2×1H, 2×s, =CH_2), 7.08 (1H, d, *J* 1.7 Hz, 4-H), 7.11 (2H, d, *J* 1.7 Hz, 2-H and 6-H), 7.39–7.42 (2H, m, 3′-H and 5′-H), 7.52 (1H, m, 4′-H) and 7.69 (2H, d, *J* 8.1 Hz, 2′-H and 6′-H); δ_C (75 MHz, $CDCl_3$) 24.3 (Me), 44.0 (CH_2), 71.1, 120.5 (=CH_2), 127.5, 128.1, 129.0, 133.1, 135.0, 141.9, 144.4, 159.9 and 180.0; *m/z* % (ES) 360 (M^++H, 2×^{35}Cl, 100); ν_{max}/cm^{-1} (film) 2930, 1818 and 1654.

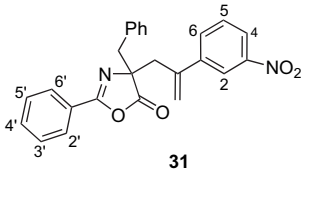
3.3.6. Methyl 4-{1-[(4-benzyl-5-oxo-2-phenyl-4,5-dihydro-1,3-oxazol-4-yl)methyl]vinyl}benzoate (30).



30

Prepared from methyl 4-iodobenzoate and 4-benzyl-2-phenyl-4*H*-oxazol-5-one by general procedure B. Column chromatography eluting with 1:1 v/v hexane–Et_2O (R_f 0.1) afforded **30** (91%) as a colourless solid, which crystallized form ether as colourless needles, mp 112–113 °C. (Found: C, 76.00; H, 5.45; N, 3.35. $C_{27}H_{23}NO_4$ requires: C, 76.20; H, 5.40; N, 3.30%.) δ_H (500 MHz, $CDCl_3$) 3.20 and 3.26 (2×1H, 2×d, J 13.4 Hz, CH_2Ph), 3.18 and 3.31 (2×1H, 2×d, J 13.8 Hz, CH_2), 3.87 (3H, s, OMe), 5.30 and 5.35 (2×1H, 2×s, =CH_2), 7.12–7.14 (5H, m, Ph), 7.27 (2H, dd, J 7.7 and 7.2 Hz, 3′-H and 5′-H), 7.29 (2H, d, J 8.1 Hz, 3-H and 5-H), 7.42 (1H, m, 4′-H), 7.47 (2H, dd, J 7.2 and 1.3 Hz, 2′-H and 6′-H) and 7.81 (2H, d, J 8.1 Hz, 2-H and 6-H); δ_C (75 MHz, $CDCl_3$) 43.1 (CH_2), 44.0 (CH_2), 52.4 (OMe), 120.3 (=CH_2), 125.7, 127.0, 127.6, 128.0, 128.5, 128.7, 129.2, 129.8, 130.5, 132.8, 134.4, 143.1, 146.0, 160.1, 167.1 (CO) and 179.3 (CO); *m/z* % (ES) 426 (M^++H, 100); ν_{max}/cm^{-1} (film) 3054, 2987, 1815, 1718 and 1657.

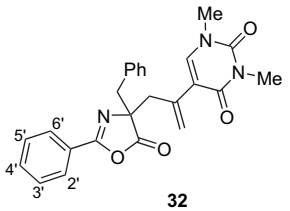
3.3.7. 4-Benzyl-4-[2-(3-nitrophenyl)prop-2-en-1-yl]-2-phenyl-1,3-oxazol-5(4*H*)-one (31).



31

Prepared from 3-nitroiodobenzene and 4-benzyl-2-phenyl-4*H*-oxazol-5-one by general procedure B. Column chromatography eluting with 4:1 v/v hexane–Et_2O (R_f 0.13) afforded **31** (80%) as a pale yellow oil. (Found: C, 72.95; H, 4.75; N, 6.65. $C_{25}H_{20}N_2O_4$ requires: C, 72.80; H, 4.85; N, 6.80%.) δ_H (500 MHz, C_6D_6) 2.84 and 2.91 (2×1H, 2×d, J 13.9 Hz, CH_2), 3.19 and 3.26 (2×1H, 2×d, J 13.4 Hz, CH_2Ph), 5.00 and 5.19 (2×1H, s, =CH_2), 6.61 (1H, dd, J 8.0 and 7.7 Hz, 5-H), 6.84–6.81 (2H, m, 3′-H and 5′-H), 6.92–6.96 (2H, m, ArH), 6.99 (1H, m, 4′-H), 7.05 (1H, d, J 7.7 Hz, 6-H), 7.20–7.17 (3H, m, ArH), 7.48 (2H, d, J 7.4 Hz, 2′-H and 6′-H), 7.65 (1H, d, J 8.0 Hz, 4-H) and 8.15 (1H, s, 2-H); δ_C (75 MHz, C_6D_6) 42.6 (CH_2), 43.5 (CH_2), 76.0, 120.4 (=CH_2), 122.2, 125.9, 127.8, 127.9, 128.3, 128.6, 128.7, 128.8, 129.0, 130.8, 132.5, 132.9, 134.8, 142.2, 143.1, 148.6, 159.8 and 178.8 (CO); *m/z* % (ES) 413 (M^++H, 100); ν_{max}/cm^{-1} (film) 3055, 2987, 1815 and 1655.

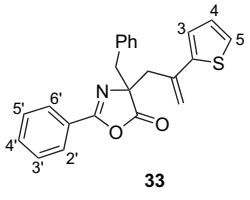
3.3.8. 5-{1-[(4-Benzyl-5-oxo-2-phenyl-4,5-dihydro-1,3-oxazol-4-yl)methyl]vinyl}-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (32).



32

Prepared from 1,3-dimethyl-5-iodouracil and 4-benzyl-2-phenyl-4*H*-oxazol-5-one by general procedure B. Column chromatography eluting with 1:1 v/v hexane–Et_2O (R_f 0.29) afforded **32** (54%) as an amorphous colourless solid, mp 58–60 °C. (Found: C, 67.30; H, 5.60; N, 9.00. $C_{25}H_{23}N_3O_4 \cdot 1H_2O$ requires: C, 67.00; H, 5.60; N, 9.40%.) HRMS found: M+H, 430.1761. $C_{25}H_{23}N_3O_4$ requires: M+H, 430.1761. δ_H (500 MHz, $CDCl_3$) 2.86 (3H, s, NMe), 3.17 and 3.24 (2×1H, 2×d, J 13.4 Hz, CH_2Ph), 3.30 (3H, s, NMe), 3.08 and 3.53 (2×1H, 2×d, J 13.8 Hz, CH_2), 5.12 and 5.18 (2×1H, 2×s, =CH_2), 6.69 (1H, s, uracil-CH), 7.11–7.15 (5H, m, Ph), 7.39–7.42 (2H, dd, J 7.8 and 7.4 Hz, 3′-H and 5′-H), 7.52 (1H, m, 4′-H) and 7.70 (2H, dd, J 7.4 and 1.2 Hz, 2′-H and 6′-H); δ_C (75 MHz, $CDCl_3$) 28.3 (Me), 36.7 (Me), 41.7 (CH_2), 44.0 (CH_2), 76.1, 115.5, 120.7 (=CH_2), 125.7, 127.6, 128.5, 129.3, 130.5, 133.2, 134.3, 138.4, 139.4, 151.5, 159.9, 162.3 (CO) and 179.1 (CO); *m/z* % (ES) 430 (M^++H, 100); ν_{max}/cm^{-1} (film) 3054, 2987, 1815, 1703 and 1659.

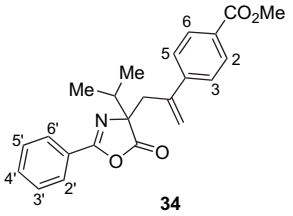
3.3.9. 4-Benzyl-2-phenyl-4-[2-(2-thienyl)prop-2-en-1-yl]-1,3-oxazol-5(4*H*)-one (33).



33

Prepared from 2-iodothiophene and 4-benzyl-2-phenyl-4*H*-oxazol-5-one by general procedure B. Column chromatography eluting with 4:1 v/v hexane–Et_2O (R_f 0.3) afforded **33** (77%) as colourless needles, mp 35–37 °C. (Found: C, 73.95; H, 5.20; N, 3.65; S, 8.65. $C_{23}H_{19}NO_2S$ requires: C, 73.95; H, 5.10; N, 3.75; S, 8.60%.) δ_H (500 MHz, $CDCl_3$) 3.20 and 3.22 (2×1H, 2×d, J 10.0 Hz, CH_2), 3.13 and 3.29 (2×1H, 2×d, J 13.8 Hz, CH_2Ph), 5.09 and 5.41 (2×1H, 2×s, =CH_2), 6.89 (1H, dd, J 5.1 and 3.8 Hz, 4-H), 7.03–7.05 (2H, m, 3-H and 5-H), 7.11–7.22 (5H, m, Ph), 7.31 (2H, dd, J 7.9 and 7.7 Hz, 3′-H and 5′-H), 7.43 (1H, m, 4′-H) and 7.61 (2H, d, J 7.9 Hz, 2′-H and 6′-H); δ_C (75 MHz, $CDCl_3$) 43.3 (CH_2), 44.0 (CH_2), 75.9, 116.8 (=CH_2), 125.0, 125.4, 126.0, 127.6, 128.1, 128.6, 128.8, 130.6, 132.7, 134.6, 136.4, 145.0, 160.2 and 179.5 (CO); *m/z* % (ES) 374 (M^++H, 100); ν_{max}/cm^{-1} (film) 3054, 2987, 1815 and 1657.

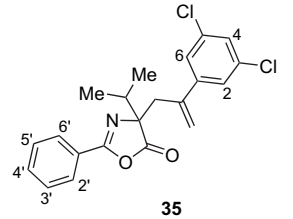
3.3.10. Methyl 4-{1-[(4-isopropyl-5-oxo-2-phenyl-4,5-dihydro-1,3-oxazol-4-yl)methyl]vinyl}benzoate (34).



34

Prepared from methyl 4-iodobenzoate and 4-isopropyl-2-phenyl-4*H*-oxazol-5-one by general procedure B at 80 °C. Column chromatography eluting with 4:1 v/v hexane–Et_2O (R_f 0.14) afforded **34** (49%) as colourless needles, mp 76–78 °C. (Found: C, 72.90; H, 6.00; N, 3.55. $C_{23}H_{23}NO_4$ requires: C, 73.15; H, 6.15; N, 3.70%.) δ_H (500 MHz, $CDCl_3$) 0.97 and 1.07 (2×3H, 2×d, *J* 6.8 Hz, 2×Me), 2.20–2.24 (1H, m, C*H*Me_2), 3.03 and 3.32 (2×1H, 2×d, *J* 13.6 Hz, CH_2), 3.87 (3H, s, OMe), 5.26 and 5.32 (2×1H, 2×s, =CH_2), 7.26–7.33 (4H, m, 3-H, 5-H, 3′-H and 5′-H), 7.46 (1H, m, 4′-H), 7.58 (2H, d, *J* 8.1 Hz, 2′-H and 6′-H) and 7.79 (2H, d, *J* 8.3 Hz, 2-H and 6-H); δ_C (75 MHz, $CDCl_3$) 17.3 (Me), 17.5 (Me), 35.7 (CH), 41.0 (CH_2), 52.4 (OMe), 119.9 (=CH_2), 125.8, 126.9, 128.1, 128.7, 129.1, 129.7, 132.8, 143.5, 146.1, 160.1, 167.1 (CO) and 179.9 (CO); *m*/*z* % (ES) 378 (M^++H, 100); ν_{max}/cm^{-1} (film) 3054, 2987, 1813, 1719 and 1657.

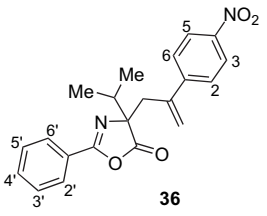
3.3.11. 4-[2-(3,5-Dichlorophenyl)prop-2-en-1-yl]-4-isopropyl-2-phenyl-1,3-oxazol-5(4*H*)-one (35).



35

Prepared from 3,5-dichloroiodobenzene and 4-isopropyl-2-phenyl-4*H*-oxazol-5-one by general procedure B at 80 °C. Column chromatography eluting with 4:1 v/v hexane–Et_2O (R_f 0.13) afforded **35** (61%) as colourless plates, mp 68–70 °C. (Found: C, 64.75; H, 4.90; N, 3.45; Cl, 18.20. $C_{21}H_{19}Cl_2NO_2$ requires: C, 64.95; H, 4.90; N, 3.60; Cl, 18.25%.) δ_H (500 MHz, $CDCl_3$) 0.97 and 1.08 (2×3H, 2×d, *J* 6.8 Hz, 2×Me), 2.19–2.25 (1H, m, C*H*Me_2), 2.97 and 3.21 (2×1H, 2×d, *J* 13.6 Hz, CH_2), 5.23 and 5.25 (2×1H, 2×s, =CH_2), 7.04 (1H, d, *J* 1.7 Hz, 4-H), 7.07 (2H, d, *J* 1.7 Hz, 2-H and 6-H), 7.37–7.45 (2H, m, 3′-H and 5′-H), 7.51 (1H, m, 4′-H) and 7.67 (2H, d, *J* 7.3 Hz, 2′-H and 6′-H); δ_C (75 MHz, $CDCl_3$) 17.3 (Me), 17.5 (Me), 35.7 (CH), 41.0 (CH_2), 77.0, 120.4 (=CH_2), 125.6, 125.7, 126.2, 127.4, 128.1, 128.9, 133.0, 134.9, 142.3, 144.7, 146.1, 160.3 and 179.7 (CO); *m*/*z* % (ES) 390 (M^++H, ^{37}Cl and ^{35}Cl, 66) and 388 (M^++H, 2×^{35}Cl, 100); ν_{max}/cm^{-1} (film) 3429, 2970, 1815, 1655 and 1292.

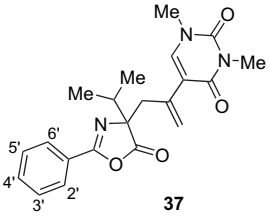
3.3.12. 4-Isopropyl-4-[2-(4-nitrophenyl)prop-2-en-1-yl]-2-phenyl-1,3-oxazol-5(4*H*)-one (36).



36

Prepared from 4-iodonitrobenzene and 4-isopropyl-2-phenyl-4*H*-oxazol-5-one by general procedure B at 80 °C. Column chromatography eluting with 4:1 v/v hexane–Et_2O (R_f 0.1) afforded **36** (59%) as colourless plates, mp 84–86 °C. (Found: C, 69.25; H, 5.70; N, 7.60. $C_{21}H_{20}N_2O_4$ requires: C, 69.20; H, 5.50; N, 7.65%.) δ_H (500 MHz, $CDCl_3$) 0.97 and 1.09 (2×3H, 2×d, *J* 6.8 Hz, 2×Me), 2.21–2.26 (1H, m, C*H*Me_2), 3.04 and 3.36 (2×1H, 2×d, *J* 13.7 Hz, CH_2), 5.35 and 5.38 (2×1H, 2×s, =CH_2), 7.27–7.34 (2H, m, 3′-H and 5′-H), 7.36 (2H, d, *J* 8.7 Hz, 2-H and 6-H), 7.47 (1H, m, 4′-H), 7.58 (2H, d, *J* 7.3 Hz, 2′-H and 6′-H) and 7.94 (2H, d, *J* 8.7 Hz, 3-H and 5-H); δ_C (75 MHz, $CDCl_3$) 17.2 (Me), 17.5 (Me), 35.7 (CH), 41.0 (CH_2), 77.1, 121.6 (=CH_2), 123.6, 125.5, 126.2, 127.4, 127.7, 127.9, 128.8, 133.1, 142.7, 147.1, 148.0, 160.2 and 179.6 (CO); *m*/*z* % (ES) 365 (M^++H, 100); ν_{max}/cm^{-1} (film) 3059, 2973, 1814 and 1656.

3.3.13. 5-{1-[(4-Isopropyl-5-oxo-2-phenyl-4,5-dihydro-1,3-oxazol-4-yl)methyl]vinyl}-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (37).



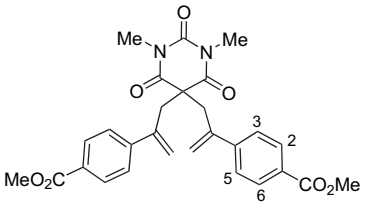
37

Prepared from 1,3-dimethyl-5-iodouracil and 4-isopropyl-2-phenyl-4*H*-oxazol-5-one by general procedure B at 80 °C. Column chromatography eluting with 1:1 hexane–Et_2O (R_f 0.06) afforded **37** (61%) as colourless plates, mp 102–103 °C. (Found: C, 65.85; H, 6.10; N, 10.95. $C_{21}H_{23}N_3O_4$ requires: C, 66.10; H, 6.05; N, 11.00%.) δ_H (500 MHz, $CDCl_3$) 0.94 and 1.05 (2×3H, 2×d, *J* 6.8 Hz, 2×Me), 2.19–2.16 (1H, m, C*H*Me_2), 2.84 (3H, s, NMe), 3.29 (3H, s, NMe), 3.55 and 2.87 (2×1H, 2×d, *J* 13.6 Hz, CH_2), 5.13 and 5.08 (2×1H, 2×s, =CH_2), 6.68 (1H, s, uracil-CH), 7.49–7.46 (2H, m, 3′-H and 5′-H), 7.57 (1H, m, 4′-H) and 7.86 (2H, d, *J* 8.2 Hz, 2′-H and 6′-H); δ_C (75 MHz, $CDCl_3$) 17.2 (Me), 17.4 (Me), 28.3 (Me), 35.8, 36.7 (Me), 115.5, 120.5 (=CH_2), 126.6, 127.8, 129.3, 133.2, 139.0, 151.5, 160.0, 162.3 (CO) and 179.1 (CO); *m*/*z* % (ES) 382 (M^++H, 100); ν_{max}/cm^{-1} (film) 3055, 2986, 1814, 1703 and 1658.

3.4. General procedure (C) for the catalytic C,C-diallylation of 1,3-dimethylbarbituric acid

Identical to procedure A except that $Pd(PPh_3)_4$ (5 mol %) was used as catalyst in acetonitrile (20 ml/1.0–3.0 mmol) at 80 °C for 20 h.

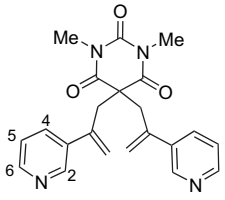
3.4.1. Dimethyl 4,4′-[(1,3-dimethyl-2,4,6-trioxohexahydropyrimidine-5,5-diyl)diprop-1-ene-3,2-diyl]dibenzoate (38).



38

Prepared from *N*,*N*′-dimethylbarbituric acid and methyl 4-iodobenzoate by general procedure C. Column chromatography eluting with 7:3 v/v petroleum ether–ethyl acetate (R_f 0.13) afforded **38** (91%) as a colourless oil. (Found: C, 66.40; H, 5.40; N, 5.60. $C_{28}H_{28}N_2O_7$ requires: C, 66.65; H, 5.60; N, 5.55%.) δ_H (500 MHz, $CDCl_3$) 2.62 (6H, s, 2×N–Me), 3.29 (4H, s, 2×CH_2), 3.88 (6H, s, 2×OMe), 5.09 and 5.18 (2×2H, 2×s, 2×=CH_2), 7.19 (4H, d, *J* 8.3 Hz, 2×3-H and 2×5-H) and 7.90 (4H, d, *J* 8.3 Hz, 2×2-H and 2×6-H); δ_C (75 MHz, $CDCl_3$) 28.1 (Me), 45.4 (CH_2), 52.5 (Me), 57.1, 120.4 (=CH_2), 127.1, 129.8, 129.9, 143.5, 144.8, 150.4 (CO), 166.8 (CO) and 170.3 (CO); *m*/*z* % (ES) 505 (M^++H, 100); ν_{max}/cm^{-1} (film) 3423, 2953, 1723, 1681 and 1608.

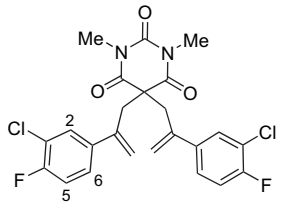
3.4.2. 1,3-Dimethyl-5,5-bis(2-pyridin-3-ylprop-2-en-1-yl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (39).



39

Prepared from *N*,*N*′-dimethylbarbituric acid and 3-iodopyridine by general procedure C. Column chromatography eluting with 9:1 v/v ethyl acetate–methanol (R_f 0.20) afforded **39** (92%) as a colourless oil. (Found: C, 67.30; H, 6.00; N, 14.10. $C_{22}H_{22}N_4O_3$ requires: C, 67.60; H, 5.60; N, 14.35%.) δ_H (500 MHz, $CDCl_3$) 2.70 (6H, s, 2×N–Me), 3.28 (4H, s, 2×CH_2), 5.11 and 5.19 (2×2H, 2×s, 2×=CH_2), 7.19 (2H, dd, *J* 7.7 and 4.8 Hz, 2×5-H), 7.47 (2H, d, *J* 7.8 Hz, 2×4-H), 8.37 (2H, s, 2×2-H) and 8.46 (2H, d, *J* 4.6 Hz, 2×6-H); δ_C (75 MHz, $CDCl_3$) 28.5 (Me), 45.1 (CH_2), 56.9, 120.5 (=CH_2), 123.6, 128.9, 129.2, 132.5, 133.5, 134.4, 135.7, 140.9, 148.1, 149.6, 150.2 (CO) and 170.2 (CO); *m*/*z* % (ES) 390 (M^+, 100); ν_{max}/cm^{-1} (film) 3602, 3085, 3033, 2959, 1747 and 1680.

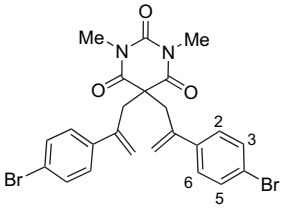
3.4.3. 5,5-Bis[2-(3-chloro-4-fluorophenyl)prop-2-en-1-yl]-1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (40).



40

Prepared from *N*,*N*′-dimethylbarbituric acid and 3-chloro-4-fluoroiodobenzene by general procedure C. Column chromatography eluting with 17:3 v/v petroleum ether–ethyl acetate (R_f 0.10) afforded **40** (94%) as a colourless solid, which crystallized from petroleum ether–ethyl acetate as colourless plates, mp 78–79 °C. (Found: C, 58.15; H, 4.20; N, 5.90; Cl, 14.25. $C_{24}H_{20}Cl_2F_2N_2O_3$ requires: C, 58.40; H, 4.10; N, 5.70; Cl, 14.35%.) δ_H (500 MHz, $CDCl_3$) 2.76 (6H, s, 2×N–Me), 3.22 (4H, s, 2×CH_2), 5.03 and 5.11 (2×2H, 2×s, 2×=CH_2), 7.00 (4H, m, 2×2-H and 2×6-H) and 7.17 (2H, dd, *J* 6.9 and 2.0 Hz, 2×5-H, where $J_{H-H} \sim J_{H-F}$); δ_C (75 MHz, $CDCl_3$) 28.2 (Me), 45.5 (CH_2), 57.0, 116.6, 116.8, 119.7 (=CH_2), 121.1, 121.3, 126.9, 127.4, 129.4, 137.5, 142.6, 150.4 (CO), 156.4, 159.7 and 173.3 (CO); *m*/*z* % (ES) 493 (M^++H, 2×^{35}Cl, 20); ν_{max}/cm^{-1} (film) 3091, 3045, 2959, 1748, 1681, 1630.

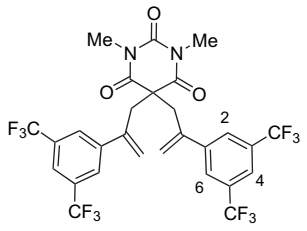
3.4.4. 5,5-Bis[2-(4-bromophenyl)prop-2-en-1-yl]-1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (41).



41

Prepared from *N*,*N*′-dimethylbarbituric acid and 4-bromoiodobenzene by general procedure C. Column chromatography eluting with 4:1 v/v petroleum ether–ether (R_f 0.18) afforded **41** (93%) as a colourless solid, which crystallized from petroleum ether–ether as colourless needles, mp 118–119 °C. (Found: C, 52.80; H, 4.25; N, 5.10; Br, 29.10. $C_{24}H_{22}Br_2N_2O_3$ requires: C, 52.75; H, 4.05; N, 5.15; Br, 29.25%.) δ_H (500 MHz, $CDCl_3$) 2.67 (6H, s, 2×N–Me), 3.22 (4H, s, 2×CH_2), 5.01 and 5.09 (2×2H, 2×s, 2×=CH_2), 6.97 (4H, d, *J* 8.3 Hz, 2×2-H and 2×6-H) and 7.36 (4H, d, *J* 8.3 Hz, 2×3-H and 2×5-H); δ_C (75 MHz, $CDCl_3$) 28.1 (Me), 45.6 (CH_2), 57.1, 119.4 (=CH_2), 122.9, 129.2, 131.7, 139.1, 143.2, 150.5 (CO) and 170.3 (CO); *m*/*z* % (ES) 549 (M^++H, 2×^{81}Br, 20); ν_{max}/cm^{-1} (film) 3083, 3045, 2951, 2880, 1747, 1680 and 1623.

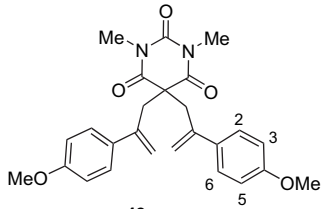
3.4.5. 5,5-Bis{2-[3,5-bis(trifluoromethyl)phenyl]prop-2-en-1-yl}-1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (42).



42

Prepared from *N*,*N*′-dimethylbarbituric acid and 3,5-bis(trifluoromethyl)iodobenzene by general procedure C. Column chromatography eluting with 9:1 v/v petroleum ether–ethyl acetate (R_f 0.15) afforded **42** (95%) as a colourless solid, which crystallized from petrol–ethyl acetate as colourless plates, mp 120–121 °C. (Found: C, 50.85; H, 3.15; N, 4.30. $C_{28}H_{20}F_{12}N_2O_3$ requires: C, 50.90; H, 3.05; N, 4.25%.) δ_H (500 MHz, $CDCl_3$) 2.68 (6H, s, 2×N–Me), 3.32 (4H, s, 2×CH_2), 5.20 and 5.27 (2×2H, 2×s, 2×=CH_2), 7.57 (4H, s, 2×2-H and 2×6-H) and 7.76 (2H, s, 2×4-H); δ_C (75 MHz, $CDCl_3$) 27.7 (Me), 44.7 (CH_2), 56.6, 123.0 (q, J_{C-F} 272.7 Hz, CF_3), 121.7 (=CH_2), 121.8, 126.8, 131.8 (q, J_{C-F} 33.5 Hz, *C*–CF_3), 141.4, 141.9, 149.6 (CO) and 169.7 (CO); *m*/*z* % (ES) 661 (M^++H, 40); ν_{max}/cm^{-1} (solid) 3421, 3107, 2964, 1810, 1749 and 1686.

3.4.6. 5,5-Bis[2-(4-methoxyphenyl)prop-2-en-1-yl]-1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (43).

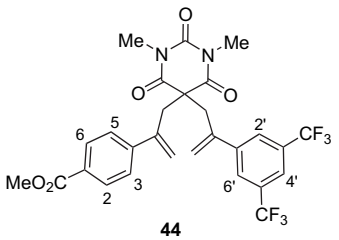


43

Prepared from *N*,*N*′-dimethylbarbituric acid and 4-iodoanisole by general procedure C. Column chromatography eluting with 17:3 v/v petroleum ether–ethyl acetate afforded **43** (89%) as a colourless oil. (Found: C, 69.70; H, 6.40; N, 6.00. $C_{26}H_{28}N_2O_5$ requires: C, 69.65; H, 6.30; N, 6.25%); δ_H (500 MHz, $CDCl_3$) 2.66 (6H, s, 2×N–Me), 3.23 (4H, s, 2×H_2), 3.75 (6H, s, 2×OMe), 4.92 and 5.01 (2×2H, 2×s, 2×=CH_2), 6.75 (4H, d, *J* 8.5 Hz, 2×3-H and 2×5-H) and 7.03 (4H, d, *J* 8.5 Hz, 2×2-H and 2×6-H); δ_C (75 MHz, $CDCl_3$) 28.1 (Me), 46.0 (CH_2), 55.6 (Me), 57.2, 113.4, 117.6 (=CH_2), 128.5, 132.6, 143.9, 150.7 (CO), 159.7 and 170.7 (CO); *m*/*z* % (ES) 449 (M^++H, 20); ν_{max}/cm^{-1} (film) 3036, 2956, 2837, 1746, 1679 and 1606.

3.4.7. Methyl 4-{1-[5-{2-[3,5-bis(trifluoromethyl)phenyl]prop-2-en-1-yl}-1,3-dimethyl-2,4,6-trioxohexahydropyrimidin-5-ylmethyl]vinyl}benzoate (44).

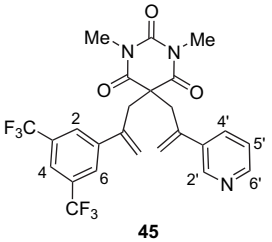
Prepared from *N*,*N*′-dimethylbarbituric acid, methyl 4-iodobenzoate and 3,5-bis(trifluoromethyl)iodobenzene by general procedure C. Column chromatography eluting with



44

4:1 v/v petroleum ether–ethyl acetate (R_f 0.17) afforded **44** (40%) as a colourless solid, which crystallized from petroleum ether–ether as colourless plates, mp 119–120 °C. (Found: C, 57.50; H, 4.15; N, 4.85. $C_{28}H_{24}F_6N_2O_5$ requires: C, 57.75; H, 4.15; N, 4.80%.) δ_H (500 MHz, $CDCl_3$) 2.65 (6H, s, 2×N–Me), 3.28 and 3.33 (2×2H, 2×s, 2×CH_2), 3.89 (3H, s, OMe), 5.13, 5.15 and 5.23 (2×1H and 1×2H, 3×s, 2×=CH_2), 7.19 (2H, d, *J* 8.1 Hz, 3-H and 5-H), 7.57 (2H, s, 2′-H and 6′-H), 7.74 (1H, s, 4′-H) and 7.93 (2H, d, *J* 8.1 Hz, 2-H and 6-H); δ_C (75 MHz, $CDCl_3$) 28.1 (Me), 44.2 (CH_2), 46.2 (CH_2), 52.6 (Me), 57.0, 120.9 (=CH_2), 121.2 (=CH_2), 121.9, 123.4 (q, J_{C-F} 272.4 Hz, CF_3), 126.9, 127.3, 130.0, 130.1, 131.75 (q, J_{C-F} 33.5 Hz, *C*–CF_3), 142.3, 142.9, 143.0, 144.2, 150.2, 166.8 (CO) and 170.2 (CO); *m*/*z* % (ES) 583 (M^++H, 100); ν_{max}/cm^{-1} (film) 3697, 3093, 2959, 1747, 1732, 1685, 1631 and 1607.

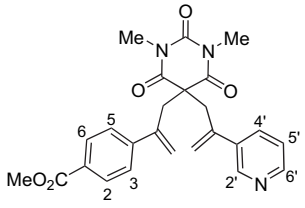
3.4.8. 5-{2-[3,5-Bis(trifluoromethyl)phenyl]prop-2-en-1-yl}-1,3-dimethyl-5-(2-pyridin-3-ylprop-2-en-1-yl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (45).



45

Prepared from *N*,*N*′-dimethylbarbituric acid, 3,5-bis(trifluoromethyl)iodobenzene and 3-iodopyridine by general procedure C. Column chromatography eluting with 3:2 v/v petroleum ether–ethyl acetate (R_f 0.23) afforded **45** (21%) as a colourless solid, which crystallized from petroleum ether–ethyl acetate as colourless plates. HRMS Found: 526.1552 (M^++H); $C_{25}H_{22}F_6N_3O_3$ requires: 526.1565. δ_H (500 MHz, $CDCl_3$) 2.70 (6H, s, 2×N–Me), 3.28 and 3.33 (2×2H, s, 2×CH_2), 5.13, 5.19, 5.21 and 5.26 (4×1H, 4×s, 2×=CH_2), 7.21 (1H, dd, *J* 7.8 and 4.8 Hz, 5′-H), 7.47 (1H, dd, *J* 7.8 and 1.6 Hz, 4′-H), 7.58 (2H, s, 2-H and 6-H), 7.75 (1H, s, 4-H), 8.37 (1H, d, *J* 1.9 Hz, 2′-H) and 8.47 (1H, d, *J* 4.7 Hz, 6′-H); δ_C (75 MHz, $CDCl_3$) 28.1 (Me), 44.6 (CH_2), 45.6 (CH_2), 56.9, 120.8 (=CH_2), 121.6 (=CH_2), 121.9, 123.3 (q, J_{C-F} 272.7 Hz, CF_3), 123.5, 127.3, 132.1 (q, J_{C-F} 33.5 Hz, *C*–CF_3), 134.3, 135.5, 140.7, 142.1, 142.6, 148.0, 149.8, 150.1 and 170.2 (CO); *m*/*z* % (ES) 526 (M^++H, 100); ν_{max}/cm^{-1} (solid) 3417, 3093, 2956, 2159, 1976, 1747, 1679 and 1624.

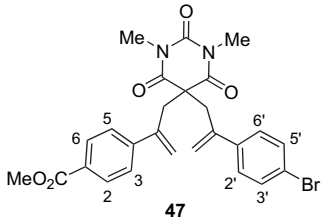
3.4.9. Methyl 4-({[1,3-dimethyl-2,4,6-trioxo-5-(2-pyridin-3-ylprop-2-en-1-yl)hexahydropyrimidin-5-yl]methyl}vinyl)benzoate (46).



46

Prepared from *N*,*N*′-dimethylbarbituric acid, methyl 4-iodobenzoate and 3-iodopyridine by general procedure C. Column chromatography eluting with 3:7 v/v petroleum ether–ethyl acetate (R_f 0.23) afforded **46** (37%) as a pale brown oil. (Found: C, 67.25; H, 5.75; N, 9.50. $C_{25}H_{25}N_3O_5$ requires: C, 67.10; H, 5.65; N, 9.40%.) δ_H (500 MHz, $CDCl_3$) 2.66 (6H, s, 2×N–Me), 3.29 (4H, s, 2×CH_2), 3.89 (3H, s, OMe), 5.09, 5.11, 5.17 and 5.21 (4×1H, 4×s, 2×=CH_2), 7.19 (3H, m, 3-H, 5-H and 5′-H), 7.48 (1H, d, *J* 7.3 Hz, 4′-H), 7.92 (2H, d, *J* 7.7 Hz, 2-H and 6-H), 8.36 (1H, s, 2′-H) and 8.45 (1H, d, *J* 3.0 Hz, 6′-H); δ_C (75 MHz, $CDCl_3$) 28.1 (Me), 44.7 (CH_2), 45.8 (CH_2), 52.5, 57.0, 120.3 (=CH_2), 120.6 (=CH_2), 123.5, 127.0, 129.9, 134.5, 135.9, 143.3, 144.5, 145.9, 148.2, 150.3 (CO), 166.8 (CO), 170.3 (CO); *m*/*z* % (ES) 448 (M^++H, 100); ν_{max}/cm^{-1} (film) 2952, 1747, 1722, 1680, 1625 and 1607.

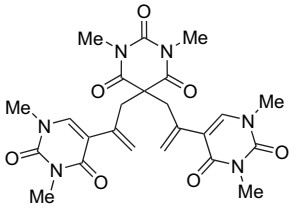
3.4.10. Methyl 4-[1-({5-[2-(4-bromophenyl)prop-2-en-1-yl]-1,3-dimethyl-2,4,6-trioxohexahydropyrimidin-5-yl}methyl)vinyl]benzoate (47).



47

Prepared from *N*,*N*′-dimethylbarbituric acid, methyl 4-iodobenzoate and 4-bromoiodobenzene by general procedure C. Column chromatography eluting with 7:3 v/v petroleum ether–ethyl acetate (R_f 0.25) afforded **47** (38%) as a colourless oil. (Found: C, 59.65; H, 5.05; N, 5.10; Br, 15.20. $C_{26}H_{25}BrN_2O_5$ requires: C, 59.45; H, 4.80; N, 5.35; Br 15.20%.) δ_H (500 MHz, $CDCl_3$) 2.65 (6H, s, 2×N–Me), 3.24 and 3.28 (2×2H, 2×s, 2×CH_2), 3.88 (3H, s, OMe), 5.02, 5.09, 5.10 and 5.18 (4×1H, 4×s, 2×=CH_2), 6.98 (2H, d, *J* 8.3 Hz, 3′-H and 5′-H), 7.18 (2H, d, *J* 8.1 Hz, 3-H and 5-H), 7.35 (2H, d, *J* 8.3 Hz, 2′-H and 6′-H) and 7.91 (2H, d, *J* 8.1 Hz, 2-H and 6-H); δ_C (75 MHz, $CDCl_3$) 28.5 (Me), 45.4 (CH_2), 45.6 (CH_2), 52.6, 57.1, 119.4 (=CH_2), 120.4 (=CH_2), 122.5, 127.7, 128.9, 129.9, 130.0, 131.7, 139.0, 143.2, 143.5, 144.8, 150.4 (CO), 166.9 (CO) and 170.3 (CO); *m*/*z* % (ES) 526 (M^+, 20, ^{81}Br); ν_{max}/cm^{-1} (film) 3087, 2952, 2851, 1723, 1679, 1608 and 1587.

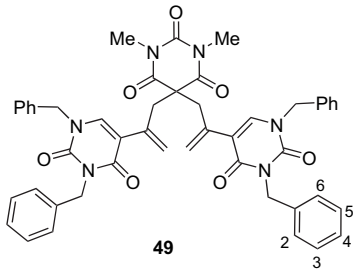
3.4.11. 5,5-Bis[2-(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)prop-2-en-1-yl]-1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (48).



48

Prepared from *N*,*N*′-dimethylbarbituric acid and 1,3-dimethyl-5-iodouracil by general procedure C. Column chromatography eluting with ethyl acetate (R_f 0.15) afforded **48** (83%) as a colourless solid, which crystallized from hexane–DCM as colourless plates, mp 158–160 °C. (Found: C, 56.25; H, 5.50; N, 16.55. $C_{24}H_{28}N_6O_7$ requires: C, 56.25; H, 5.50; N, 16.40%.) δ_H (500 MHz, $CDCl_3$) 3.03 (6H, s, 2×N–Me), 3.15 (4H, s, 2×CH_2), 3.31 (6H, s, 2×N–Me), 3.35 (6H, s, 2×N–Me), 5.08, 5.16 (2×2H, s, 2×=CH_2) and 6.87 (2H, s, 2×uracil-CH); δ_C (75 MHz, $CDCl_3$) 28.1 (Me), 30.9 (Me), 36.9, 44.7, 57.1, 113.5, 121.2, 135.9, 139.8, 150.7, 151.1, 161.6 (CO) and 170.4 (CO); *m*/*z* % (ES) 513 (M^++H, 100); ν_{max}/cm^{-1} (film) 3516, 3062, 2954, 1746 and 1653.

3.4.12. 5,5-Bis[2-(1,3-dibenzyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)prop-2-en-1-yl]-1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (49).



49

Prepared from *N*,*N*′-dimethylbarbituric acid and 1,3-dibenzyl-5-iodouracil by general procedure C. Column chromatography eluting with 3:2 v/v petroleum ether–ethyl acetate (R_f 0.18) afforded **49** (79%) as a colourless solid, which crystallized from petroleum ether–ethyl acetate as colourless plates, mp 76–78 °C. (Found: C, 70.30; H, 5.45; N, 10.35. $C_{48}H_{44}N_6O_7$ requires: C, 70.55; H, 5.40; N, 10.30%.) δ_H (500 MHz, $CDCl_3$) 2.74 (6H, s, 2×N–Me), 3.13 (4H, s, 2×CH_2), 4.85 (4H, s, 2×CH_2Ph), 5.01 (2×1H, s, 2×=CH_2), 5.10 (2×1H and 2×2H, s, 2×=CH_2 and 2×CH_2Ph), 6.84 (2H, s, 2×uracil-CH), 7.46 (4H, d, *J* 7.2 Hz, 2×2-H and 2×6-H), 7.33–7.38 (6H, m, 2×3-H, 2×4-H and 2×5-H) and 7.25–7.31 (10H, m, 2×Ph); δ_C (75 MHz, $CDCl_3$) 21.2, 27.9 (Me), 44.1, 44.8, 52.4, 57.0, 114.1, 121.4, 127.6, 128.4, 128.4, 128.6, 129.1, 129.2, 134.9, 135.9, 136.6, 138.7, 150.4, 151.0, 161.2 (CO) and 170.3 (CO); *m*/*z* % (ES) 817 (M^++H, 80); ν_{max}/cm^{-1} (film) 3064, 3033, 2953, 1747, 1703, 1679 and 1654.

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