Synthetic routes to pyrrolizine-1,5-dione derivatives by flash vacuum pyrolysis of amidomethylene derivatives of Meldrum's acid†

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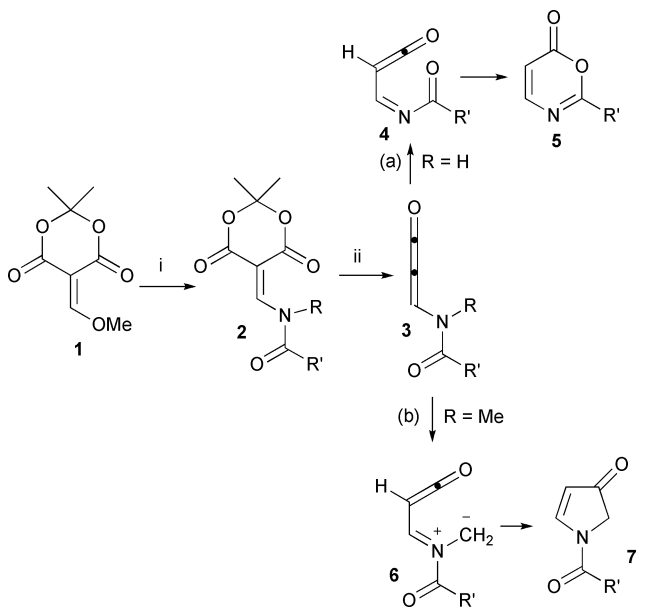
Methoxymethylene Meldrum's acid **1** reacts with 5- and 6-membered lactams in refluxing acetonitrile to give the *N*-substituted products **9–15**. If the reactions are continued for extended times, the Meldrum's acid derivatives decompose to provide enamidoesters *e.g.* **22–24**. Flash vacuum pyrolysis of the 5-membered ring products **9–13** provides reasonable yields of the fused pyrrolones **31–35**. The constitution of the products is supported by X-ray crystal structures of **10**, **12**, **19**, **32** and **34**.

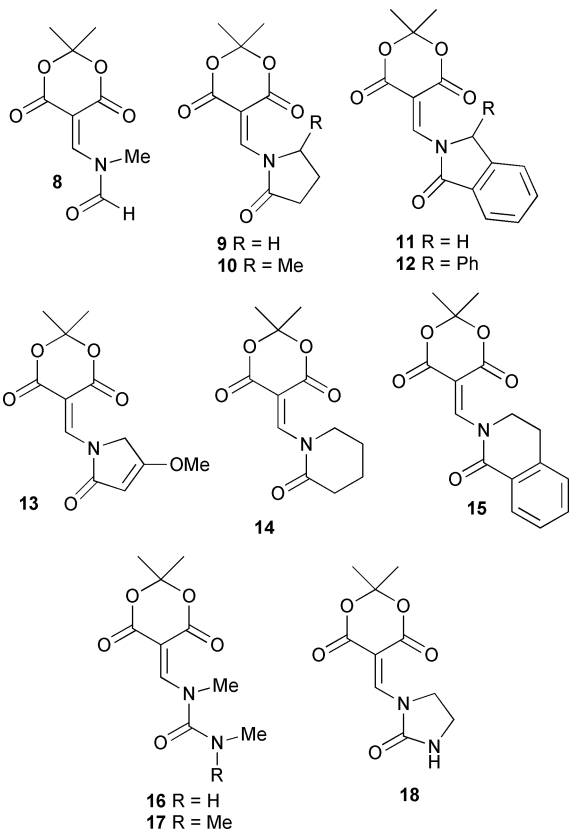
Introduction

In previous work[1] we have shown that primary amides can act as *N*-nucleophiles in their reactions with methoxymethylene Meldrum's acid **1**, though long reaction times in refluxing acetonitrile may be required. Flash vacuum pyrolysis (FVP) of the products **2** (R = H) provides a useful synthetic route to 1,3-oxazin-6-ones **5**, *via* methyleneketene **3** and imidoylketene intermediates **4** [Scheme 1, route (a)].[2]



Scheme 1 *Reagents and conditions*: (i) R′CONHR, CH_3CN, reflux; (ii) FVP 500–550 °C.

An alternative cyclisation mechanism takes place when methylene Meldrum's acid derivatives derived from secondary amines are subjected to FVP, leading to *N*-substituted 1*H*-pyrrol-3(2*H*)-ones (or 3-hydroxypyrroles).[2,3] However, the cyclisation does not proceed when various *N*-protected derivatives are pyrolysed.[4,5]



The purpose of the work described in this paper was to extend the reactions of **1** with amides, to secondary amides and lactams, and to explore the pyrolysis reactions of the resulting derivatives **2** (R = alkyl). It was hoped that the 'normal' reaction of the *N*,*N*-disubstituted methyleneketene **3** (*e.g.* R = Me) would lead to a dipolar intermediate[6] **6** which could collapse to a protected pyrrolone **7** [Scheme 1, route (b)]. In principle, deprotection could lead to *N*-unsubstituted pyrrolones and, with appropriate substituents, provide complementary entry to the prodigiosin series of antibiotics.[7,8] Clearly the presence of an *N*-electron withdrawing group might destabilise the dipolar intermediate **6**,

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but we have evidence that the cyclisation to **7** may be relatively insensitive to electronic effects in the dipole.[9]

Results and discussion

The reaction of methoxymethylene Meldrum's acid **1** with secondary amides proved to be sensitive to the structure of the amide and to the reaction time. Most acylic amides (*e.g. N*-methylacetamide or *N*-methylbenzamide) failed to react and only *N*-methylformamide gave the required product **8** (57%). Reactions of **1** with five-membered (Experimental section) and six-membered (ESI†) lactams were more successful and the derivatives **9–15** were obtained in 59–90% yield, typically after 8 h reflux in acetonitrile. No derivatives of these types have been previously synthesised. The regiochemistry of the reaction was confirmed by X-ray crystallography of **10** and **12** (Fig. 1 and 2). In both cases, the methyl group of the (boat-shaped) Meldrum's acid ring is orientated on the same side of the molecule as the substituent on the lactam ring. Indeed the presence of one methyl group of **12** in the shielding zone of the phenyl substituent is reflected in its chemical shift (δ_H 0.81) by comparison with the equivalent signal in **11** (δ_H 1.75).

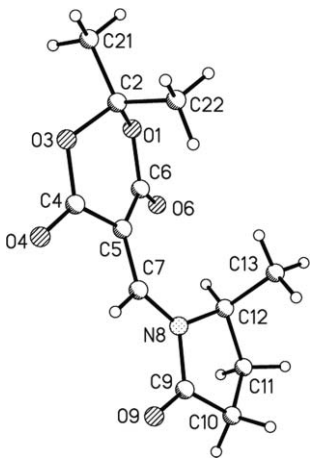


Fig. 1 Plot of **10** showing crystallographic numbering scheme.

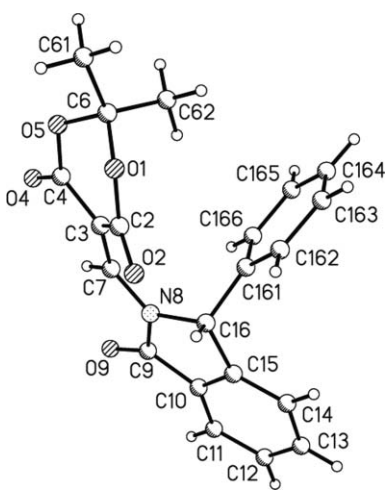
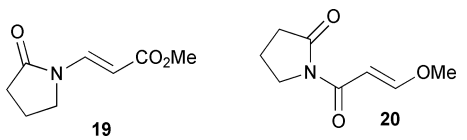


Fig. 2 Plot of **12** showing crystallographic numbering scheme.

The crystal structures show the effect of the two conjugative electron withdrawing groups (the lactam carbonyl group and the methylene Meldrum's acid moiety) competing for the lone pair of the nitrogen atom. Thus, by comparison with the structure of 2,3-dihydro-3-phenylisoindol-1-one itself,[10] the C–N bond of the lactam function in **12** is lengthened from 1.346(2) to 1.427(2) Å. Correspondingly, there is less delocalisation in the Meldrum's acid region of the molecule by comparison with the *N*,*N*-dimethylaminomethylene derivative.[11] For example, this is reflected in the increase in single bond character of the C–N bond [from 1.307(4) Å to 1.351(2) Å (**10**) and 1.349(2) Å (**12**)] and increase in double bond character of the C=C bond [from 1.387(4) Å to 1.364(2) Å (**10**) and 1.359(2) Å (**12**)].

Reaction of 4-methoxy-3-pyrrolin-2-one with **1** to give **13** was more facile than the reactions of the other lactams, and proceeded at room temperature, though again long reaction times were needed. On the other hand, 6-methylpiperidin-2-one and 6-phenylpiperidin-2-one failed to react, presumably for steric reasons. Cyclic and acyclic ureas successfully provided **16–18** (10–58%) (ESI†). It is clear that these reactions lie at the limit of reactivity of **1** and a relatively minor increase in conformational and/or steric constraints can affect the success or failure of the process.



In an attempt to increase yields, the effect of extended reaction times (72–192 h) on the reaction of **1** with lactams was investigated. Surprisingly, the Meldrum's acid derivatives **8–10** (Experimental section) and **14–18** (ESI†) proved to be unstable under these conditions and alternative decomposition products were isolated in low-moderate yield. Taking the reaction of **9** as an example, structures **19** or **20** were consistent with the spectroscopic data (Experimental section) but the products were established as enamidoesters **19** and **21–27** by X-ray crystallography of **19** (Fig. 3). These products are formed by reaction of **8–10**, **14–18** with methanol, generated from the original substitution, at the 4(6)-position of the Meldrum's acid ring, followed by loss of acetone and decarboxylation. The low yields may be due to adventitious loss of methanol from the refluxing acetonitrile during the reaction. Products of this type have been made previously, *e.g.* by selective Wittig reactions of imides.[12] Trimethyl 1,3,5-benzenetricarboxylate **28** was also obtained consistently as a very minor by-product, presumably formed by trimerisation

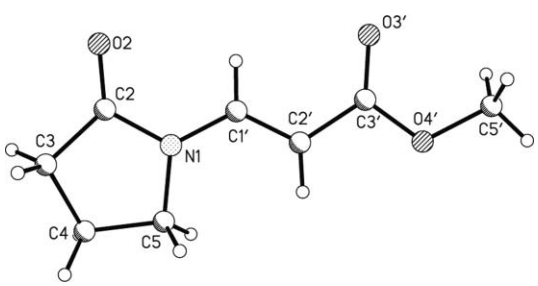
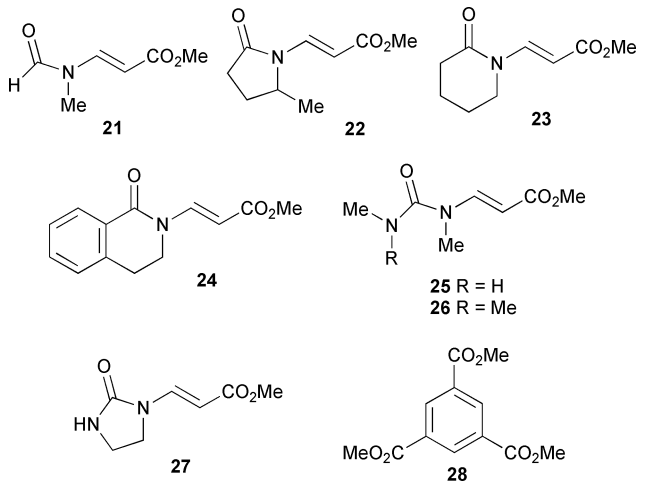


Fig. 3 Plot of **19** showing crystallographic numbering scheme.

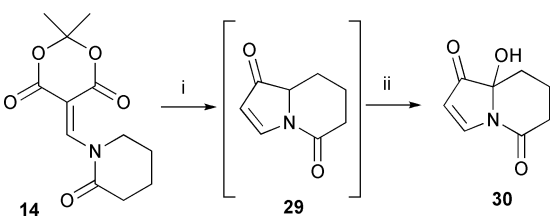
of a methyl formylacetate equivalent obtained from **1**. Related reactions have been reported.[13]

The enaminoester unit of **19** is planar (mean deviation from best plane of N1–C1′–C2′–C3′–O3′–O4′ 0.0085 Å; maximum deviation at C1′, 0.0215 Å); the bond lengths in the propenoate chain show evidence of delocalisation, but less so than in corresponding *N*,*N*-disubstituted enaminals.[14]



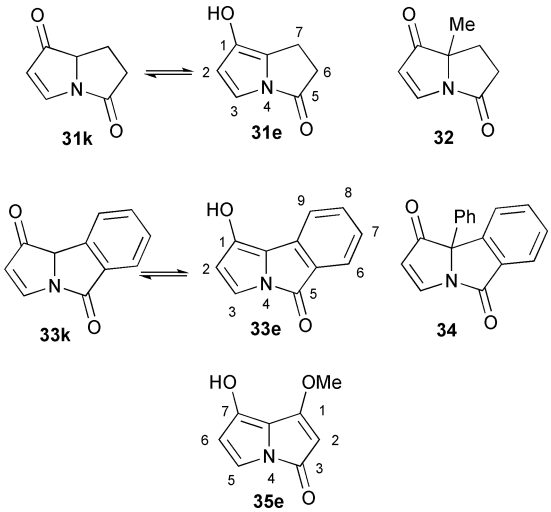
Under FVP conditions, no significant yields of cyclisation products were obtained by pyrolysis of the *N*-formyl compound **8** or the six-membered lactam derivative **15** or the ureas **16–18** (ESI†). Reasons for this behaviour are unclear, but the high migration aptitude of carbonyl derivatives[15] in potential sigmatropic shifts across the methyleneketene π-system may be involved.

A very small amount (14%) of the indolizinedione **30** was obtained by FVP of **14** at 700 °C, followed by chromatography. This suggests that the cyclisation outlined in Scheme 1 [(route (b)] can indeed take place but that the primary pyrolysis product **29** is highly prone to autoxidation (Scheme 2). It is known that the 2-position of 1*H*-pyrrol-3(2*H*)-ones (particularly those which are 2-mono-substituted) is particularly prone to autoxidation (*c.f.* ref. 16).



Scheme 2 *Reagents and conditions*: (i) FVP 700 °C; (ii) O_2.

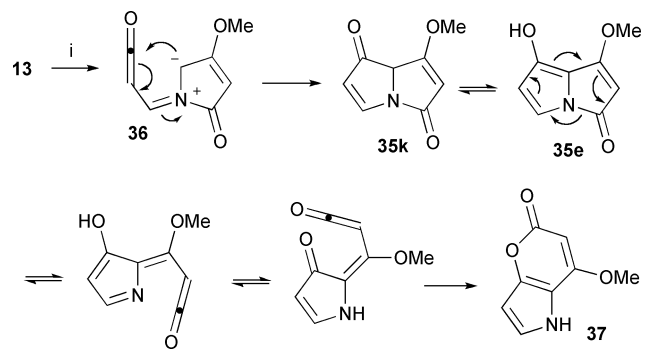
In contrast to these disappointing results, FVP reactions of the 5-membered ring substrates **9–13** all proceeded as shown in Scheme 1 [route (b)] to provide the fused pyrrolones **31–35**, respectively. The optimum temperature for the pyrolysis differed with the substrate, with formation of **31–33** requiring 700 °C (62–80%), whereas conversion to **34** was complete at 600 °C (65%).



Almost nothing is known of systems related to **31–34** at the appropriate oxidation level, though one heavily substituted analogue of **32** is known[17] together with some *O*-substituted analogues of **33**.[18] The chemical properties of the systems **31–34** will be reported in a subsequent paper.

FVP of **13** was more complex, with the pyrrolizinone **35** the major product at low temperatures (550–570 °C, 33%). This thermal cyclisation provides an unusual route to a fully unsaturated pyrrolizin-3-one system in which the key step is the creation of the 7–7a bond.[19] Some 1,2-dihydro examples have been made by an intramolecular Wittig process[20] and 7–7a bond formation is a popular route to saturated pyrrolizidin-3-ones.[21]

At higher temperatures, the pyrano[3,2-*b*]pyrrole **37** was the major product from FVP of **13** *e.g.* 650 °C (44%). It is probably formed by electrocyclic ring opening of the enol form of the pyrrolizinone **35e**, leading to a ketene intermediate, which, after tautomerism of the hydroxypyrrole, can electrocyclise to the pyrano[3,2-*b*]pyrrole **37** as the thermodynamic product of the energy surface (Scheme 3).



Scheme 3 *Reagents and conditions*: (i) FVP 550–650 °C.

The constitutions of **32** and **34** were established by X-ray crystallography (Fig. 4 and 5, respectively). Unlike the structures of pyrrolones[22,23] and pyrrolizinones[24] the stereochemistry at the nitrogen atom is forced out of plane by the sp^3 carbon atom at the bridgehead, as shown by the side views in Fig. 4 and 5.

The angle between the two 'butterfly' planes of **32** N4–C8–C1–C2–C3 (mean deviation from best plane, 0.0386 Å; maximum deviation 0.0582 Å at C1) and C8–N4–C5, is 143.4°. The

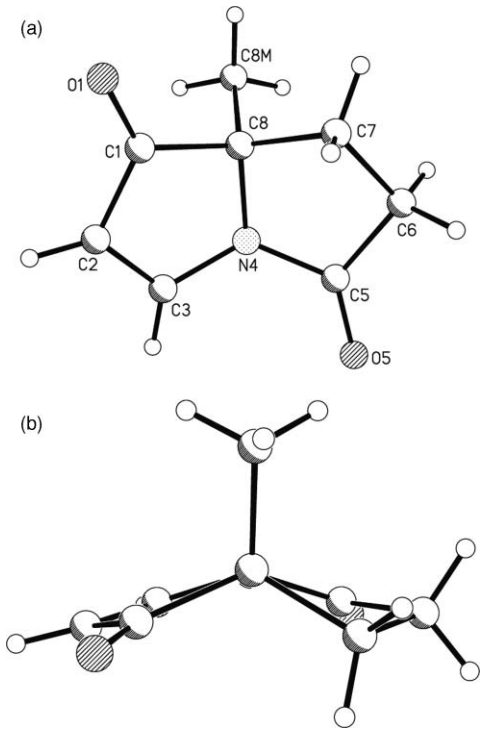


Fig. 4 Plot of **32** showing the crystallographic numbering scheme, and a side view showing the non-planarity.

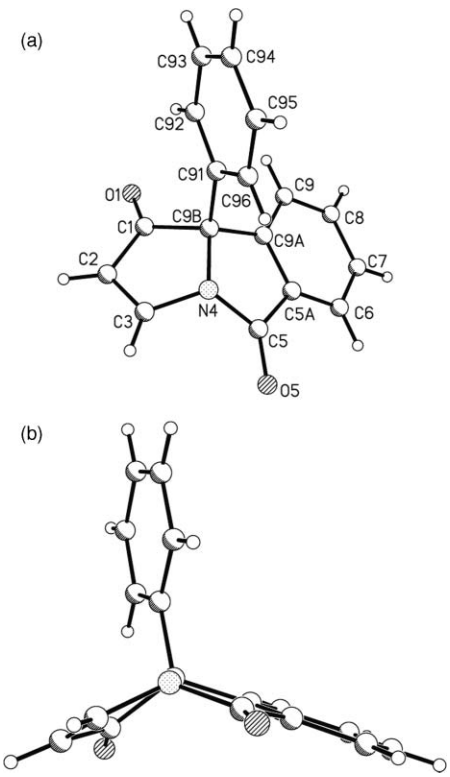


Fig. 5 Plot of **34** showing the crystallographic numbering scheme, and a side view showing the non-planarity.

corresponding angle in **34** between planes C1–C2–C3–N4–C9B (mean deviation from best plane, 0.0582 Å; maximum deviation 0.0858 Å at C9B) and N4–C5–C5A–C6–C7–C8–C9–C9A–C9B (mean deviation from best plane, 0.0098 Å; maximum deviation 0.0290 Å at C5A) is 131.6°. Comparison of the C–N bond length of the lactam unit of **32** [1.389(2) Å] with the 1,2-dihydropyrrolizin-3-one **38** [1.392(2) Å] (Fig. 6) suggests that the enaminone unit of **32** is comparable in electron withdrawing ability with a pyrrole ring. The formal single bonds of the enaminone unit of **32** and **34** are much longer than in the pyrrol-3-one model compound **39** (Fig. 6), indicating less delocalisation in the enaminone system due to competition with the lactam.

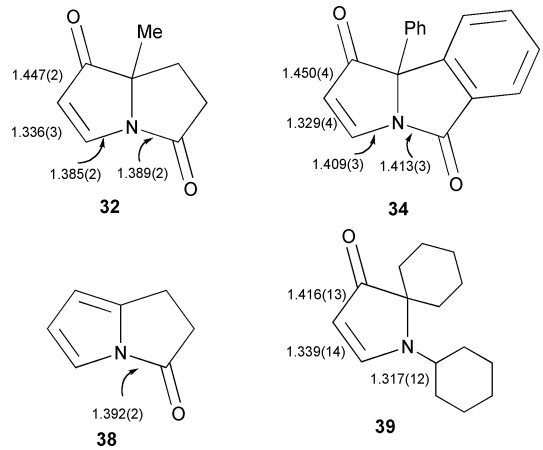


Fig. 6 Comparison of selected bond lengths (Å) of **32**, **34**, **38** and **39**.

Pyrrol-3(2*H*)-ones with a hydrogen atom at the 2-position generally exist as solvent-dependent mixtures of keto (k) and enol (e) tautomers;[23] therefore, compounds **31**, **33** and **35** are also potentially tautomeric. The pyrrolizinedione **31** is insoluble in non-polar solvents (which might be expected to favour the keto form) and in [$^2H_6$]DMSO exists entirely in the enol form **31e**. In [$^2H_4$]methanol, *ca.* 20% of the keto form **31k** could be identified by the characteristic widely spaced doublets [δ_H 5.6 and 8.1, ^3J 4.0 Hz) due to H(2) and H(3), respectively]. The benzo-analogue **33** was entirely enol **33e** in [$^2H_6$] acetone solution; taken together with the results for **31**, this suggests that these fused diones may relatively favour their enol tautomers, by comparison with *N*-aryl or *N*-alkyl pyrrolones.[23] Compound **35** exists entirely as the enol **35e** in order to maintain the conjugation of the pyrrolizin-3-one system.

Conclusions

In this paper, we have shown that most lactams can react with methoxymethylene Meldrum's acid under forcing conditions and that the 5-membered lactams are successfully transformed into pyrrolizinedione derivatives by FVP at 600–700 °C. Although the synthetic route to *N*-acylpyrrolones is not a general one, it is nevertheless a straightforward method to unusual pyrrolizinones and their benzo-derivatives. The influence of the lactam function might be expected to affect the chemistry of the pyrrolone moiety and this aspect will be explored in a subsequent paper.

Experimental

^1H and ^{13}C NMR spectra were recorded at 200 (or 250) and 50 (or 63) MHz respectively for solutions in [^2H]chloroform unless

otherwise stated. Coupling constants are quoted in Hz. Mass spectra were recorded under electron impact conditions unless otherwise stated.

Reaction of 5-methoxymethylene Meldrum's acid with lactams or ureas—Method A

The appropriate amide or lactam (10 mmol) was dissolved in acetonitrile (50 cm^3) and 5-methoxymethylene Meldrum's acid **1** (1.86 g, 10 mmol) was added. The mixture was heated under reflux for the time stated and then the solvent was removed under reduced pressure to give the product which could be recrystallised. The following Meldrum's acid derivatives were prepared. The amide or lactam used and reflux time for each example are given in parentheses.

2,2-Dimethyl-5-(*N*-formyl-*N*-methylaminomethylene)-1,3-dioxane-4,6-dione 8

(*N*-Methylformamide, 17 h) gave 2,2-dimethyl-5-(*N*-formyl-*N*-methylaminomethylene)-1,3-dioxane-4,6-dione **8** (57%), mp 141–142 °C (from hexane/toluene), (Found: C, 50.65; H, 5.45; N, 6.5. $C_9H_{11}NO_5$ requires C, 50.7; H, 5.2; N, 6.55%); δ_H 8.73 (1H, s), 8.44 (1H, s), 3.39 (3H, s) and 1.73 (6H, s); δ_C 164.58, 163.44 (quat), 158.64 (quat), 154.37, 104.22 (quat), 96.04 (quat), 33.94 and 26.92; *m/z* 213 (M^+, 3%), 156 (14), 155 (18), 128 (29), 127 (30), 99 (26), 84 (21), 83 (100), 82 (81), 81 (13) and 59 (12).

2,2-Dimethyl-5-[*N*-(2-oxopyrrolidin-1-yl)methylene]-1,3-dioxane-4,6-dione 9

(Pyrrolidin-2-one, 8 h) gave 2,2-dimethyl-5-[*N*-(2-oxopyrrolidin-1-yl)methylene]-1,3-dioxane-4,6-dione **9** (74%), mp 134–135 °C (from hexane/toluene), (Found: C, 55.4; H, 5.75; N, 5.8. $C_{11}H_{13}NO_5$ requires C, 55.25; H, 5.5; N, 5.85%); δ_H 8.69 (1H, s), 4.06 (2H, m), 2.59 (2H, t, ^3J 8.1), 2.23–2.10 (2H, m) and 1.71 (6H, s); δ_C 175.90 (quat), 163.67 (quat), 159.23 (quat), 147.20, 103.93 (quat), 94.73 (quat), 49.51, 29.58, 26.88 and 18.04; *m/z* 181 [$(M - C_3H_6O)^+$, 100%], 153 (36), 138 (11), 109 (65), 108 (21), 82 (17), 81 (61), 80 (29) and 68 (16).

2,2-Dimethyl-5-[*N*-(5-methyl-2-oxopyrrolidin-1-yl)methylene]-1,3-dioxane-4,6-dione 10

(5-Methylpyrrolidin-2-one, 8 h) gave 2,2-dimethyl-5-[*N*-(5-methyl-2-oxopyrrolidin-1-yl)methylene]-1,3-dioxane-4,6-dione **10** (67%), mp 139–140 °C (from hexane/toluene), (Found: C, 56.95; H, 6.2; N, 5.5. $C_{12}H_{15}NO_5$ requires C, 56.9; H, 5.95; N, 5.55%); δ_H 8.62 (1H, s), 5.28 (1H, m), 2.73–2.50 (2H, m), 2.28 (1H, m), 1.83 (1H, m), 1.70 (3H, s), 1.68 (3H, s) and 1.10 (3H, d, ^3J 6.4); δ_C 175.62 (quat), 163.77 (quat), 159.17 (quat), 145.89, 103.77 (quat), 94.65 (quat), 54.66, 28.12, 27.20, 26.41, 24.89 and 19.17; *m/z* 195 [$(M - C_3H_6O)^+$, 100%], 167 (17), 149 (11), 123 (44), 122 (83), 96 (54), 95 (26), 94 (43), 81 (15), 68 (33) and 67 (28).

2,2-Dimethyl-5-[*N*-(1-oxo-2,3-dihydroisoindol-2-yl)methylene]-1,3-dioxane-4,6-dione 11

[2,3-Dihydroisoindol-1(1*H*)-one,[25] 6 h] gave 2,2-dimethyl-5-[*N*-(1-oxo-2,3-dihydroisoindol-2-yl)methylene]-1,3-dioxane-4,6-dione **11** (60%), mp 196–197 °C (dec.) (from toluene/ethyl acetate), (Found: C, 62.45; H, 4.75; N, 4.6. $C_{15}H_{13}NO_5$ requires C, 62.7; H, 4.55; N, 4.9%); δ_H 9.04 (1H, s), 7.97 (1H, m), 7.73 (1H, m), 7.57–7.50 (2H, m), 5.29 (2H, s) and 1.75 (6H, s); δ_C 167.79 (quat), 163.80 (quat), 159.82 (quat), 146.95, 142.96 (quat), 135.47, 129.02, 126.92 (quat), 125.77, 123.37, 104.04 (quat), 94.51 (quat), 52.42 and 27.03; *m/z* 287 (M^+, 4%), 280 (26), 231 (31), 230 (68), 229 (100), 202 (37), 201 (70), 186 (64), 185 (77), 157 (85), 149 (62), 133 (71) and 104 (75).

5-(1*H*-2,3-Dihydro-1-oxo-3-phenylisoindol-2-yl)methylene-2,2-dimethyl-1,3-dioxane-4,6-dione 12

(2,3-Dihydro-3-phenyl-1*H*-isoindol-1-one,[26] 19 h, followed by a second equivalent of **1**, 6 h) gave 5-(1*H*-2,3-dihydro-1-oxo-3-phenylisoindol-2-yl)methylene-2,2-dimethyl-1,3-dioxane-4,6-dione **12** (62%) mp 238–239 °C (from acetonitrile) (Found: C, 69.4; H, 4.7; N, 3.85. $C_{21}H_{17}NO_5$ requires C, 69.45; H, 4.55; N, 4.1%); δ_H 8.93 (1H, s), 8.01 (1H, d, ^3J 7.6), 7.63 (1H, td, ^3J 7.5 and ^4J 1.3), 7.50 (1H, t, ^3J 7.5), 7.32–7.20 (4H, m), 7.09–7.05 (2H, m), 6.94 (1H, s), 1.55 (3H, s) and 0.81 (3H, s); δ_C 167.88 (quat), 163.25 (quat), 160.25 (quat), 148.08 (quat), 144.97, 135.67, 135.59 (quat), 129.22, 129.05, 128.74, 127.47, 125.51, 123.52, 103.93 (quat), 97.19 (quat), 65.09, 27.18 and 24.93; *m/z* (FAB), 364 [$(M + H)^+$, 14%].

5-[1-(4-Methoxy-2-oxo-3-pyrrolin-1-yl)]methylene-2,2-dimethyl-1,3-dioxane-4,6-dione 13

Using a slightly different procedure, a solution of 5-methoxymethylene-2,2-dimethyl-1,3-dioxane-4,6-dione **1** (1.86 g, 10 mmol) and 4-methoxy-3-pyrrolin-2-one (1.13 g, 10 mmol) in acetonitrile (10 cm^3) was stirred at room temperature for 48 h and the solvent removed to give 5-[1-(4-methoxy-2-oxo-3-pyrrolin-1-yl)]methylene-2,2-dimethyl-1,3-dioxane-4,6-dione **13** (2.41 g, 90%), mp 211 °C (from ethanol) (Found: C, 54.15; H, 5.0; N, 5.3. $C_{12}H_{13}NO_6$ requires C, 53.95; H, 4.85; N, 5.25%); δ_H 8.86 (1H, s), 5.30 (1H, s), 4.78 (2H, s), 3.96 (3H, s) and 1.72 (6H, s); δ_C 179.22 (quat), 169.44 (quat), 164.04 (quat), 160.17 (quat), 145.95, 103.81 (quat), 91.68 (quat), 59.26, 52.34 and 26.93 (CH_3), *m/z* 210 [$(M - C_3H_5O)^+$, 100%], 202 (78), 158 (22), 132 (20), 96 (32), 69 (31) and 41 (37).

Reaction of 5-methoxymethylene Meldrum's acid 1 with lactams or ureas—Method B

If the reflux conditions used in Method A were extended to the times quoted below, the Meldrum's acid derivative **1** reacted with methanol to give enamidoesters, which were isolated by either dry flash column chromatography (eluting with *n*-hexane and ethyl acetate) or recrystallisation. The following compounds were prepared. The cyclic amide used, reflux time and method of isolation are given in parentheses.

Methyl 3-(*N*-formyl-*N*-methylamino)prop-2-enoate 21

(*N*-Methylformamide, 75 h, chromatography) gave methyl 3-(*N*-formyl-*N*-methylamino)prop-2-enoate **21** (11%), mp 85–86 °C (from ethanol), (Found: C, 49.95; H, 6.75; N, 9.5. $C_6H_9NO_3$ requires C, 50.35; H, 6.35; N, 9.8%); δ_H 8.42 (1H, s), 7.76 (1H, d, ^3J 13.5), 5.36 (1H, d, ^3J 13.5), 3.68 (3H, s) and 3.01 (3H, s);

δ_C 166.98 (quat), 162.98, 143.52, 99.22, 51.29 and 27.47; *m/z* 143 (M^+, 26%), 125 (37), 115 (56), 112 (41) and 84 (100).

Methyl 3-[*N*-(2-oxopyrrolidin-1-yl)]prop-2-enoate 19

(Pyrrolidin-2-one, 72 h, chromatography) gave methyl 3-[*N*-(2-oxopyrrolidin-1-yl)]prop-2-enoate **19** (19%), mp 83–84 °C (from hexane/toluene), (Found: C, 56.95; H, 6.85; N, 8.15. $C_8H_{11}NO_3$ requires C, 56.8; H, 6.55; N, 8.3%); δ_H 8.01 (1H, d, ^3J 14.3), 5.13 (1H, d, ^3J 14.3), 3.65 (3H, s), 3.49 (2H, t, ^3J 7.2), 2.47 (2H, t, ^3J 7.8) and 2.15–2.05 (2H, m); δ_C 174.02 (quat), 167.34 (quat), 137.14, 99.85, 51.08, 44.65, 30.62 and 17.10; (NMR data consistent with published spectra[27]) *m/z* 169 (M^+, 100%), 138 (37), 137 (13), 114 (8), 110 (42), 82 (49) and 70 (17).

Methyl 3-[*N*-(5-methyl-2-oxopyrrolidin-1-yl)]prop-2-enoate 22

(5-Methylpyrrolidin-2-one, 138 h, chromatography) gave methyl 3-[*N*-(5-methyl-2-oxopyrrolidin-1-yl)]prop-2-enoate **22** (26%), bp 105 °C (0.7 Torr), (Found: M^+, 183.0907. $C_9H_{13}NO_3$ requires *M*, 183.0895); δ_H 7.93 (1H, d, ^3J 14.5), 5.21 (1H, d, ^3J 14.5), 4.00 (1H, m), 3.66 (3H, s), 2.63–2.16 (3H, m), 1.74 (1H, m) and 1.21 (3H, d, ^3J 6.4); δ_C 173.73 (quat), 167.51 (quat), 136.18, 99.85, 51.09, 52.23, 29.15, 25.60 and 17.63; *m/z* 183 (M^+, 68%), 168 (42), 152 (69), 151 (27), 124 (95), 108 (17), 96 (100), 83 (20) and 70 (34).

All of these reactions consistently produced the same by-product in small amounts (30–100 mg) which could be isolated from the column, always eluting first. This was identified as trimethyl 1,3,5-benzenetricarboxylate **28** mp 140–141 °C (lit.,[28] 141–142 °C); δ_H 8.81 (3H, s) and 3.94 (9H, s); δ_C 165.19 (quat), 134.37, 131.01 (quat) and 52.44; *m/z* 252 (M^+, 10%), 222 (6), 221 (43), 193 (6), 44 (42) and 40 (100).

FVP experiments

The substrate was volatilised into the furnace tube (35 × 2.5 cm) and the products were collected in a U-tube trap cooled by liquid nitrogen situated at the exit point of the furnace. Quantity of substrate, furnace temperature (T_f), inlet temperature (T_i), background pressure (P) and reaction time (t) are specified. After pyrolysis, involatile solid products were scraped from the trap, whereas volatile solids and liquids were washed from the trap with solvent. After the solvent had been removed under reduced pressure, the crude pyrolysate was purified by either recrystallisation, Kugelrohr distillation or dry flash column chromatography (using ethyl acetate and *n*-hexane as eluents).

FVP of 2,2-dimethyl-5-[*N*-(2-oxopiperidinyl)methylene]-1,3-dioxane-4,6-dione 14

FVP of **14** [1.27 g (5.0 mmol), T_f 700 °C, T_i 195 °C, P 0.02 Torr, t 90 min] produced a complex mixture that was subjected to dry flash chromatography using *n*-hexane and ethyl acetate as eluents. The only identifiable product obtained was 8a-hydroxy-7,8-dihydroindolizine-1,5(6*H*,8a*H*)-dione **30** (0.12 g, 14%), bp 120 °C (0.3 Torr), (Found: M^+, 167.0588. $C_8H_9NO_3$ requires *M*, 167.0582); δ_H 8.48 (1H, d, ^3J 4.4), 5.57 (1H, d, ^3J 4.4), 2.88 (1H, m), 2.65–2.06 (3H, m), 1.86 (1H, m) and 1.42 (1H, m); δ_C 201.42 (quat), 168.17 (quat), 154.89, 106.80, 84.63 (quat), 29.88, 27.50 and 15.45; *m/z* 167 (M^+, 8%), 139 (67), 111 (68), 96 (65), 86 (56), 85 (47), 84 (100), 83 (84), 82 (52) and 68 (75).

7-Hydroxy-1,2-dihydropyrrolizin-3(2*H*)-one 31

FVP of 2,2-dimethyl-5-[*N*-(2-oxopyrrolidin-1-yl)methylene]-1,3-dioxane-4,6-dione **9** [1.79 g (7.5 mmol) T_f 700 °C, T_i 170 °C, P 0.02 Torr, t 150 min] produced 7-hydroxy-1,2-dihydropyrrolizin-3(2*H*)-one **31** which was purified by recrystallisation, (62%), mp 149–150 °C (dec.) (from ethyl acetate/methanol), (Found: C, 61.1; H, 5.1; N, 9.95. $C_7H_7NO_2$ requires C, 61.3; H, 5.15; N, 10.2%); δ_H ([$^2H_6$]DMSO) 8.57 (1H, s), 6.79 (1H, d, ^3J 3.1), 6.09 (1H, d, ^3J 3.1), and 2.95–2.75 (4H, m); δ_C ([$^2H_6$]DMSO) 171.71 (quat), 137.89 (quat), 118.28 (quat), 113.01, 108.09, 34.43 and 17.83; *m/z* 137 (M^+, 98%), 109 (16), 108 (19), 96 (20), 95 (100), 81 (17), 80 (38), 68 (15) and 67 (29).

7a-Methyl-7,7a-dihydro-6*H*-pyrrolizine-1,5-dione 32

FVP of 2,2-dimethyl-5-[*N*-(5-methyl-2-oxopyrrolidin-1-yl)methylene]-1,3-dioxane-4,6-dione **10** [1.91 g (7.2 mmol), T_f 700 °C, T_i 180 °C, P 0.01 Torr, t 90 min] gave 7a-methyl-7,7a-dihydro-6*H*-pyrrolizine-1,5-dione **32** (0.74 g, 68%), which was purified by Kugelrohr distillation [bp 145 °C (0.2 Torr)], mp 91–92 °C. (Found: C, 63.35; H, 5.95; N, 9.1. $C_8H_9NO_2$ requires C, 63.55; H, 6.0; N, 9.25%); δ_H 8.11 (1H, d, ^3J 4.0), 5.56 (1H, d, ^3J 4.0), 2.92 (1H, ddd, ^2J 17.4, ^3J 12.7 and 8.1), 2.53 (1H, dd, ^2J 17.4 and ^3J 7.7), 2.10–1.88 (2H, m) and 1.41 (3H, s); δ_C 205.27 (quat), 172.45 (quat), 152.99, 111.64, 69.09 (quat), 34.40, 27.56 and 22.09; *m/z* 151 (M^+, 100%), 123 (27), 122 (17), 95 (43), 82 (19), 81 (60), 80 (32), 68 (26) and 67 (72).

1-Hydroxypyrrolo[2,1-*a*]isoindol-5-one 33

FVP of 2,2-dimethyl-5-[*N*-(1-oxo-2,3-dihydroisoindol-2-yl)methylene]-1,3-dioxane-4,6-dione **11** [0.80 g (2.8 mmol), T_f 700 °C, T_i 165 °C, P 0.01 Torr, t 180 min] produced 1-hydroxypyrrolo[2,1-*a*]isoindol-5-one **33** which was purified by recrystallisation, (0.41 g, 80%), mp 100–101 °C (from chloroform/hexane). (Found: C, 71.1; H, 4.1; N, 7.8. $C_{11}H_7NO_2$ requires C, 71.35; H, 3.8; N, 7.55%); δ_H ([$^2H_6$]acetone) 9.02 (1H, br s), 7.60–7.39 (3H, m), 7.15 (1H, m), 6.95 (1H, d, ^3J 3.4) and 5.95 (1H, d, ^3J 3.4); δ_C ([$^2H_6$]acetone) 160.86 (quat), 142.39 (quat), 135.24 (quat), 133.46, 129.63 (quat), 124.34 (2CH), 118.35, 115.53, 114.50 (quat) and 110.17; *m/z* 185 (M^+, 100%), 157 (18), 133 (24), 132 (13), 130 (10), 129 (12), 104 (12), 103 (18), 102 (12) and 76 (11).

9b-Phenyl-9b*H*-pyrrolo[2,1-*a*]isoindole-1,5-dione 34

FVP of 5-(1*H*-2,3-dihydro-1-oxo-3-phenylisoindol-2-yl)methylene-2,2-dimethyl-1,3-dioxane-4,6-dione **12** [(0.5 g (1.4 mmol), T_f 600 °C, T_i 275 °C, P 0.01–0.1 Torr, t 4 h] gave 9b-phenyl-9b*H*-pyrrolo[2,1-*a*]isoindole-1,5-dione **34** (0.24 g, 65%) which was purified by recrystallisation, mp 110–112 °C (from hexane/toluene) (Found: C, 78.15; H, 4.2; N, 5.4. $C_{17}H_{11}NO_2$ requires C, 78.1; H, 4.2; N, 5.4%); δ_H 8.44 (1H, d, ^3J 4.0), 7.87–7.80 (2H, m), 7.79–7.62 (3H, m), 7.48 (1H, td, ^3J 7.6 and ^4J 1.0), 7.38–7.17 (3H, m) and 5.84 (1H, d, ^3J 4.0); δ_C 197.27 (quat), 168.83 (quat), 157.32, 145.22 (quat), 137.22 (quat), 135.11, 130.61 (quat), 128.86, 128.66,

125.58, 124.96, 123.50, 116.17 and 75.18 (quat); *m/z* (FAB) 262 [(M + H)$^+$, 84%].

FVP of 5-[1-(4-methoxy-2-oxo-3-pyrrolin-1-yl)]methylene-2,2-dimethyl-1,3-dioxane-4,6-dione 13

The product mixture was found to contain two major isomeric components. The relative proportion of these isomers was strongly temperature dependent. At the lower temperatures (550–570 °C) [*e.g.* 0.180 g, (0.67 mmol). T_f 565 °C, T_i 160 °C, P 0.02 Torr, t 120 min] a yellow solid was produced together with a small quantity of unreacted starting material. The yellow solid was scraped from the trap and identified as 7-hydroxy-1-methoxypyrrolizin-3-one **35** (0.036 g, 33%), (decomposes on heating) (Found: C, 58.0; H, 4.55; N, 8.35. $C_8H_7NO_3$ requires C, 58.2; H, 4.25; N, 8.5%); δ_H (360 MHz, [$^2H_6$]acetone) 9.46 (1H, br s), 6.88 (1H, d, ^3J 3.2), 5.74 (1H, dd, ^3J 3.2 and ^6J 0.8), 4.72 (1H, d, ^6J 0.8), and 3.93 (3H, s); δ_C ([$^2H_6$]acetone) 117.74, 105.91, 86.22, and 57.44 (non-quaternary signals only); *m/z* 165 (M$^+$, 62%), 122 (13) and 58 (100).

At higher temperatures (570–700 °C) but otherwise similar pyrolysis parameters, the pyrrolizin-3-one **35** was formed together with 7-methoxy-1*H*-pyrano[3,2-*b*]pyrrol-5-one **37**, (0.049 g, 44%), a less volatile red solid which condensed near the exit point of the furnace (decomposes on heating). (Found: M$^+$ 165.043. $C_8H_7NO_3$ requires *M*, 165.043); δ_H ([$^2H_6$]acetone) 10.88 (1H, br s), 7.16 (1H, m), 6.11 (1H, m), 5.36 (1H, s), and 4.00 (3H, s); δ_C ([$^2H_6$]acetone) 163.43 (quat), 161.06 (quat), 146.41 (quat), 135.39 (quat), 122.12, 95.17, 82.05 and 54.90; *m/z* 165 (M$^+$, 100%), 151 (6), 107 (18), 94 (11) and 69 (11).

Crystal structures

Diffraction data were collected using Cu-Kα radiation on a Stoe Stadi-4 diffractometer. Structures were solved by direct methods and refined by full-matrix least squares against F^2 (SHELXTL).[29] H-atoms were placed in ideal positions and allowed to ride on their parent atoms. Non-H atoms were modelled with anisotropic displacement parameters. Crystallographic data for the compounds reported in this paper are available on the Cambridge Database. REFCODES are **10** (OCAVAQ), **12** (OCARUG), **19** (OCAVEU), **32** (OCASOB) and **34** (OCAREQ). A table of crystal and refinement statistics is available in Table 1 in the ESI.†

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