Cyclisation reactions of some pyridazinylimidoylketenes†

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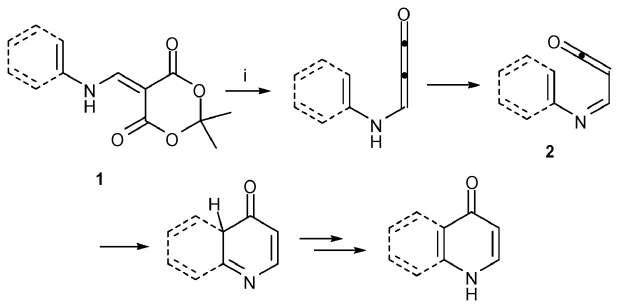
Flash vacuum pyrolysis (FVP) of aminopyridazinone derivatives of Meldrum's acid at 600 °C (0.02 Torr) results in generation of an imidoylketene intermediate followed by cyclisation. In the case of the 5-amino derivatives, the products are pyrido[2,3-*d*]pyridazines, whereas the 4-amino compounds lead to mixtures of pyrido[2,3-*d*]pyridazines and pyrrolo[3,2-*c*]pyridazines. The feasibility of the 1,5-sigmatropic shift of a chlorine atom, required for the formation of two of the pyrido[2,3-*d*]pyridazines, was supported by the corresponding reaction of a corresponding 2,6-dichloroaniline derivative. The feasibility of the decarboxylation mechanism required for the formation of the pyrrolo[3,2-*c*]pyridazines, was supported by related processes in the FVP reactions of model compounds and by DFT calculations.

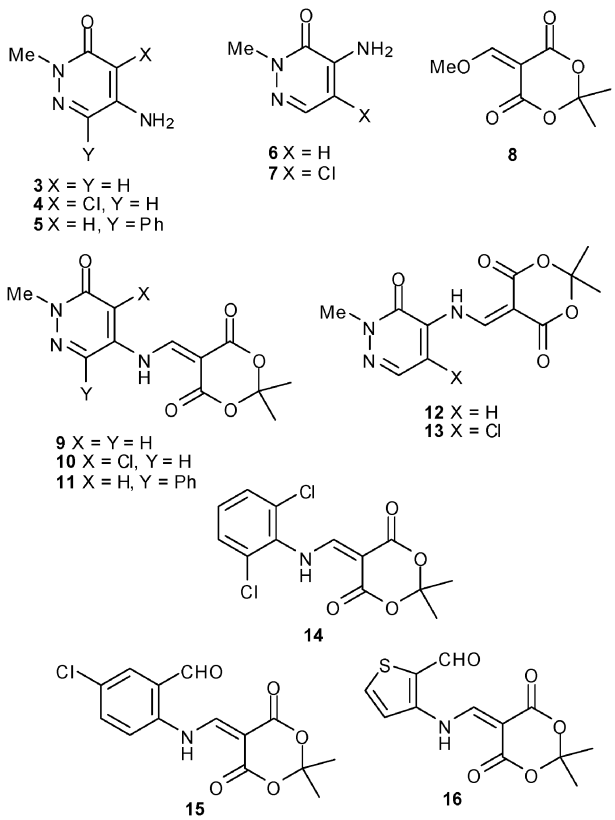
Introduction

The electrocyclisation reactions of imidoylketene intermediates **2**, generated by thermolysis of aminomethylene derivatives of Meldrum's acid **1** in solution or under flash vacuum pyrolysis (FVP) conditions, provide an important route to fused pyridin-4-one derivatives (Scheme 1).[1] The method has been applied to alkene substrates (leading to pyridin-4-ones),[2] to benzenoid substrates (leading to quinolin-4-ones),[3] to polycyclic derivatives (leading to certain marine alkaloids)[4] and to heterocyclic substrates.[3a]

In the latter context, we noted that, with the availability of the aminopyridazinones **3–7**,[5–8] it might be possible to use the Meldrum's acid strategy to access some unusual ring systems comprising fused quinolinone and pyridazinone moieties. No dione systems of this type are known, though some triones have been reported.[9,10]



Scheme 1 *Reagents and conditions:* (i) heat [either in solution (*e.g.* Dowtherm, 220 °C) or by FVP (*e.g.* 600 °C, 0.02 Torr)].



We discuss the results of these studies in this paper, which have led not only to the expected pyridopyridazines, but also to the discovery of an unexpected halogen-induced sigmatropic shift and an unusual decarboxylation mechanism leading to the pyrrolo-[3,2-*c*]pyridazine ring system. The proposed mechanisms for these new transformations are supported by DFT calculations.

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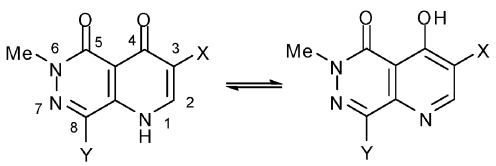
† Electronic supplementary information (ESI) available: Experimental, Cartesian coordinates, calculated energies and negative frequencies of species in Fig. 1 and Fig. 2 and spectra. See DOI: 10.1039/b9nj00474b

Results and discussion

Treatment of the pyridazines **3–7** with methoxymethylene Meldrum's acid **8** gave the aminomethylene derivatives **9–13** in 56–92% yields. Compounds **14–16** were made similarly from the corresponding arylamines; 3-aminothiophene-2-carbaldehyde,[11] required for making **16**, was obtained from the corresponding 2-carboxylic ester by a reduction–oxidation sequence (see ESI†).

FVP at 600 °C of the Meldrum's acid derivatives **9–11**, derived from the 5-aminopyridazinones, all gave single products in 70–96% yields, which condensed at the exit point of the furnace. Their mass spectra supported the formation of the expected pyrido[2,3-*d*]pyridazine ring system. For solubility reasons, the phenyl derivative **19** was the best characterised of the three. Its ^{1}H NMR spectrum shows $^3J_{2,3}$ 5.3 and 5.5 Hz in d_6-DMSO and $CDCl_3$, respectively; its ^{13}C NMR spectrum shows quaternary signals at δ_C (d_6-DMSO) 166.2 and 162.5 due to the two C–O moieties. These data suggest that **19** adopts the enol form **19e** as the major tautomer, since the coupling constant $^3J_{2,3}$ in typical pyridin-4-ones (such as **22**) is larger, and the chemical shift of the keto carbonyl [C(4)] in such derivatives would be expected at around δ_C 175–180 (*c.f.***22**; δ_C 175.3). The enol form is likely to be stabilised by intramolecular hydrogen bonding. Microwave pyrolysis of **11** provided an alternative route to **19** which avoids the use of FVP conditions.



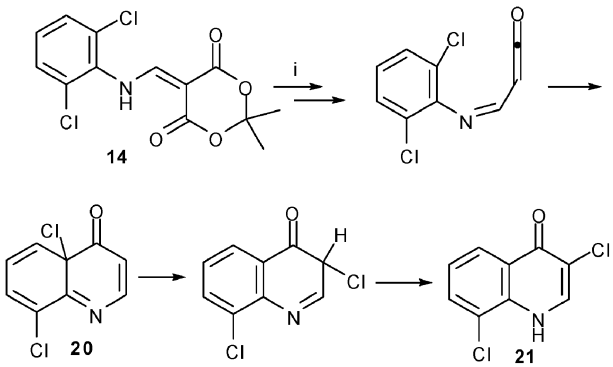
17k X = Y = H
18k X = Cl, Y = H
19k X = H, Y = Ph

17e X = Y = H
18e X = Cl, Y = H
19e X = H, Y = Ph

The ^{1}H NMR spectrum of **17** showed broad signals, presumably due to keto–enol exchange, which could be sharpened by addition of a drop of TFA to the solution (ESI†). The coupling constant of the sharpened spectrum ($^3J_{2,3}$ 5.9 Hz) is again consistent with the enol tautomer **17e** predominating.

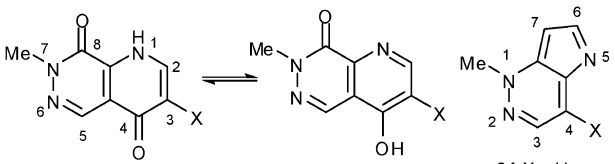
The mass spectrum of the product obtained by FVP of **10** showed that the chlorine atom had been retained, even though it was located on the cyclisation site, but the product was too insoluble for solution-phase NMR spectra. It is likely that this product is **18**, in which the chlorine atom has undergone a 1,5-sigmatropic shift to the 3-position during the reaction. The feasibility of this rearrangement process was demonstrated by FVP of **14** (Scheme 2) which provided 3,8-dichloroquinolin-4(1*H*)-one **21** (54%) as the major product, *via* sigmatropic shift of Cl in the initial cyclisation intermediate **20** and final tautomerisation. Examples of the participation of chlorine atoms in sigmatropic shifts have been reported.[12]

FVP of both the 4-aminopyridazinone derivatives **12** and **13** at 600 °C gave poorly soluble white solids which condensed at the exit point of the furnace, but in addition, both gave more volatile, chloroform-soluble yellow solids as co-products. A repeat pyrolysis at 850 °C showed the two products were



Scheme 2 *Reagents and conditions:* (i) FVP (600 °C, 0.03 Torr).

formed in a similar ratio. The non-volatile materials were easily identified from mass and NMR spectra as the expected pyrido[2,3-*d*]pyridazines **22** and **23**, respectively. In this case both the coupling constant ($^3J_{2,3}$ 7.5 Hz) and chemical shift of the C(4) carbonyl group (δ_C 175.3) of **22** suggest that the compound adopts the keto tautomer **22k**, in common with most pyridin-4-one systems.[13] The location of the chloro-substituent in **23** could be unambiguously assigned as the 3-position, owing to the absence of a signal in the range δ_H 6.0–6.5, expected for the 3-proton of pyridin-4-one systems.[14] These results lend further support to the assigned structure of **18** and the mechanism of Scheme 2.



22k X = H
23k X = Cl

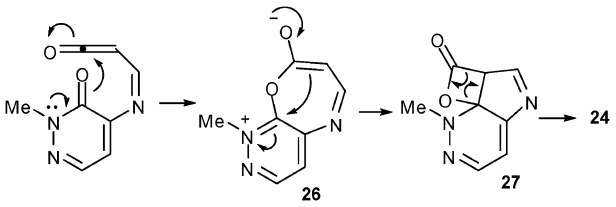
22e X = H
23e X = Cl

24 X = H
25 X = Cl

The more volatile products from FVP of **12** and **13** were shown by mass spectrometry to have resulted from loss of the elements of CO_2 from the imidoylketene, which suggests that, at some stage in the sequence, the ketene carbonyl group bonds to the carbonyl of the pyridazinone. The pyridazinone ring apparently remains intact in these products, but the coupling constants of the remaining two protons (δ_H 8.5 and 6.5 ppm) were 2.0–2.2 Hz, typical of pyrrole-type protons. These products were therefore identified as the pyrrolo[3,2-*c*]-pyridazines **24** and **25** (see ESI†). There are only 4 references to pyrrolo[3,2-*c*]pyridazines in the open literature, none of which adopt the 1*H*-tautomer.[15–18]

As one possible mechanism for the formation of **24** (and **25**), cyclisation of the carbonyl group into the appropriate imidoylketene could lead to the formation of a dipolar intermediate **26**. This can undergo an electrocyclisation to give the β-lactone **27** which leads to the pyrrolopyridazine by decarboxylation (Scheme 3). In addition, it is likely that the 5-position of the pyridazinone is deactivated by the electron-withdrawing carbonyl group, reducing the formation of **22**.

Although other mechanisms can be drawn, the feasibility of the proposed schemes was supported by DFT calculations at the B3LYP/6-31G** level[19] and the energy surface obtained is



Scheme 3

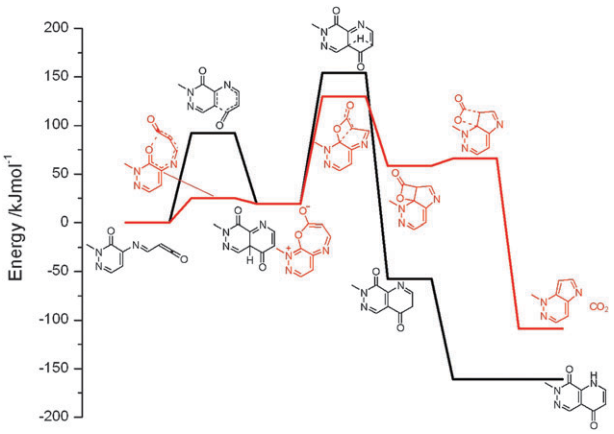


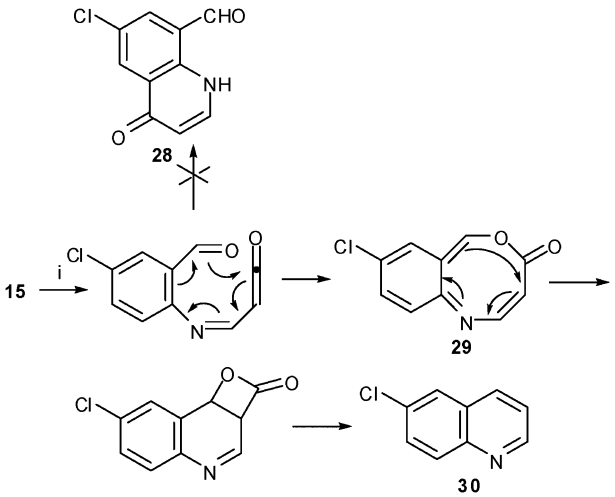
Fig. 1 Energy surface for the formation of compounds **22** and **24**.

shown in Fig. 1. The electrocyclisation mechanism to give **22** (shown in black) follows a similar pattern to other examples of this reaction[20,21] with an initial barrier to the electrocyclisation (92.2 kJ mol^{-1}), followed by the rate determining 1,5-hydrogen shift with a larger energy barrier (135.1 kJ mol^{-1}). As previously reported,[21] the 1,3-hydrogen shift to the final product could not be modelled and may take place on the surface of the furnace tube or in the solid-state after condensation.

The electrocyclisation–decarboxylation mechanism to give **24** (shown in red) has a small barrier (25.3 kJ mol^{-1}) to form the dipolar intermediate **26**. Formation of the β-lactone tricycle **27** has a barrier of 110.5 kJ mol^{-1}, and decarboxylation has a barrier of 7.7 kJ mol^{-1} to give the product **24** and carbon dioxide. Hence the calculated activation energies for the electrocyclisation–decarboxylation mechanism leading to **24** are lower than for the standard electrocyclisation mechanism leading to **22**, suggesting that the process is under kinetic control at 600 °C.

The key structural feature leading to the decarboxylation mechanism is a carbonyl group in the β-position relative to the imidoylketene moiety. The substrates **15** and **16** were therefore designed to explore whether a similar decarboxylation process could take place in a slightly different environment. In the case of **15**, normal cyclisation at the 6-position could take place to provide 8-formyl-6-chloroquinolin-4-one **28**. In practice, FVP of **15** at 600 °C gave 6-chloroquinoline **30** (62%) as the only significant product; the proposed mechanism (Scheme 4) is analogous to that of Scheme 3, though an eight-membered ring intermediate **29** is involved.

The calculated[19] energy surface for the formation of 6-chloroquinoline **30** from the aminobenzaldehyde precursor by the mechanism of Scheme 4 (Fig. 2) also establishes that the proposed mechanism is feasible under FVP conditions. The initial electrocyclisation has an energy barrier of 91 kJ mol^{-1},



Scheme 4 *Reagents and conditions:* (i) FVP (600 °C, 0.01 Torr).

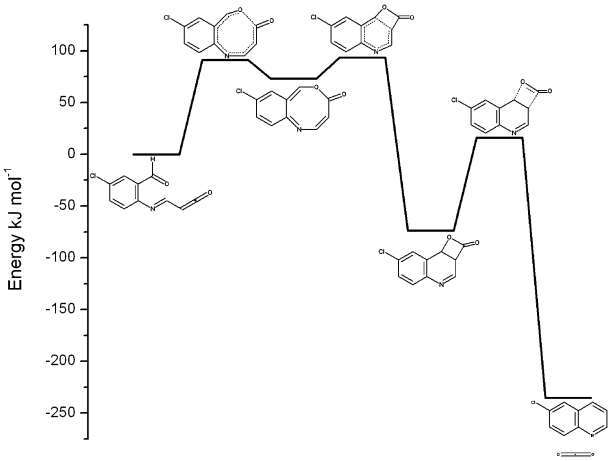
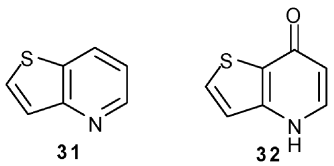


Fig. 2 Energy surface for the formation of 6-chloroquinoline **30**.

which leads to an intermediate 73 kJ mol^{-1} higher than the initial imidoylketene. However, the second electrocyclisation proceeds *via* a barrier of only 20 kJ mol^{-1} to give the β-lactone, 74 kJ mol^{-1} lower in energy than the imidoylketene. Decarboxylation proceeds *via* a 90 kJ mol^{-1} barrier to give the two products, which have a combined energy that is 235 kJ mol^{-1} lower than that of the initial ketene and providing a large thermodynamic driving force for the decarboxylation to occur.

Finally, FVP of the thiophene derivative **16** gave two products which were identified as the thienopyridine **31** (formed by an analogous mechanism to that of Scheme 4) in 57% isolated yield at 850 °C. The second product (1 : 1 ratio with **31** at 550 °C) was the thienopyridinone **32**, in which cyclisation at the aldehyde site of the thiophene (*c.f.* Scheme 1) is followed by concomitant aromatisation and decarbonylation. Other examples of cleavage (and migration) of *ortho*-substituents in related systems will be reported in a future paper.



Conclusions

Although the FVP of reactions of the pyridazinone derivatives **9** and **11** proceeded in standard fashion, two new reactions of imidoylketene derivatives have been discovered during the course of this work. In the first place, the 1,5-sigmatropic shift of the chlorine atom in **10** and **13** has apparently not been previously observed in imidoylketene intermediates. Second, the decarboxylation mechanism observed with compounds **12**, **13**, **15** and **16** is of interest mechanistically and provides a new synthetic route to the unusual pyrrolo[3,2-*c*]pyridazine ring system.

Experimental

The ^{1}H and ^{13}C NMR spectra were recorded in d_6-DMSO or in $CDCl_3$ on spectrometers operating at 250, 360, 400 or 600 MHz for protons. Chemical shifts are quoted relative to TMS, coupling constants are quoted in Hertz. ^{13}C NMR signals refer to one CH resonance unless otherwise stated. The IR spectra were obtained using potassium bromide pellets; microwave reactions were carried out in a single mode microwave apparatus. Mass spectra were recorded under electron impact conditions.

Compounds **3**,[5]**4**,[6]**5**,[7]**6**[8] and **7**[6] were prepared according to the literature procedures. Other reagents and solvents were purchased from commercial sources and used without further purification.

Aminomethylene Meldrum's acid derivatives—general procedures

Method 1. A mixture of crude methoxymethylene Meldrum's acid **8** and the appropriate pyridazine **3–7** (3 mmol) in ethanol (10 ml) was stirred at temperature *T* for time *t*, then allowed to cool to room temperature. The precipitate formed (**9–13**) was filtered off, washed with ethanol and dried *in vacuo* (50 °C, 25 Torr).

Method 2. Methoxymethylene Meldrum's acid **8** (1 equivalent) was added to a solution of the amine (1 equivalent) in the minimum volume of acetonitrile. Unless otherwise stated, the mixture was allowed to stand for 15 min and the solvent removed to give the product.

The following products were made by these methods:

2,2-Dimethyl-5-[(1-methyl-6-oxo-1,6-dihydropyridazin-4-ylamino)methylene]-1,3-dioxane-4,6-dione 9

Reaction of **3** and **8** using Method 1 gave **9** (*T* 35 °C; *t* 6 h) as an off-white solid (92%), mp 227.6–228.8 °C. (Found: C, 51.4; H, 4.45; N, 14.95. $C_{12}H_{13}N_3O_5$ requires C, 51.6; H, 4.7; N, 15.05%). δ_H (d_6-DMSO) 11.01 (1H, d, ^{3}J 14.0), 8.59 (1H, d, ^{3}J 14.0), 8.29 (1H, d, ^{4}J 2.5), 7.06 (1H, d, ^{4}J 2.5), 3.62 (3H, s) and 1.68 (6H, s); δ_C (d_6-DMSO) 163.2 (quat), 162.1 (quat), 159.7 (quat), 153.3, 141.6, 130.8, 111.6, 104.5 (quat), 90.3 (quat), 39.2 (CH_3) and 26.6 ($2CH_3$) (one quat not assigned); ν_{max} 3164, 3090, 3054, 2984, 2948, 1736, 1688, 1664, 1620, 1598, 1534, 1460, 1428, 1386, 1272, 1202, 1024, 994, 928, 896, 834, 772 and 730 cm^{-1}.

5-[(5-Chloro-1-methyl-6-oxo-1,6-dihydropyridazin-4-ylamino)methylene]-2,2-dimethyl-1,3-dioxane-4,6-dione 10

Reaction of **4** and **8** using Method 1 (*T* 50 °C; *t* 4 h) gave **10** as a white solid (56%), mp 214.6–216.0 °C. (Found: C, 46.0; H, 3.6; N, 13.3. $C_{12}H_{12}ClN_3O_5$ requires C, 45.95; H, 3.85; N, 13.4%.) δ_H (d_6-DMSO) 11.44 (1H, d, ^{3}J 13.4), 8.95 (1H, d, ^{3}J 13.4), 8.72 (1H, s), 3.71 (3H, s) and 1.71 (6H, s); δ_C (d_6-DMSO) 164.8 (quat), 161.5 (quat), 156.3 (quat), 153.3, 137.1 (quat), 127.8, 117.8 (quat), 105.3 (quat), 91.4 (quat), 40.4 (CH_3) and 26.6 ($2CH_3$); ν_{max} 3900, 3834, 3804, 3746, 3712, 3674, 3650, 3420, 3104, 2958, 2926, 2862, 1728, 1630, 1538, 1462, 1348, 1266, 1104, 1074, 1036, 908, 880, 800 and 732 cm^{-1}.

2,2-Dimethyl-5-[(1-methyl-6-oxo-3-phenyl-1,6-dihydropyridazin-4-ylamino)methylene]-1,3-dioxane-4,6-dione 11

Reaction of **5** and **8** using Method 1 (*T* 50 °C; *t* 4 h) provided **11** as an off-white solid (80%), mp 207.6–208.0 °C. (Found: C, 59.65; H, 4.55; N, 11.55. $C_{18}H_{17}N_3O_5$ requires C, 60.85; H, 4.8; N, 11.85%.) δ_H (d_6-DMSO) 10.83 (1H, d, ^{3}J 13.4), 8.71 (1H, d, ^{3}J 13.4), 7.59–7.51 (5H, m), 7.37 (1H, s), 3.69 (3H, s) and 1.63 (6H, s); δ_C (d_6-DMSO) 164.2 (quat), 161.6 (quat), 159.7 (quat), 153.6, 140.2 (quat), 140.1 (quat), 131.8 (quat), 129.8, 129.0 (4CH), 111.2, 104.8 (quat), 90.6 (quat), 39.4 (CH_3) and 26.5 ($2CH_3$); ν_{max} 3424, 3230, 1732, 1696, 1662, 1612, 1582, 1506, 1396, 1280, 1226, 1198, 1056, 998, 924, 884, 790, 748 and 708 cm^{-1}.

2,2-Dimethyl-5-[(2-methyl-3-oxo-2,3-dihydropyridazin-4-ylamino)methylene]-1,3-dioxane-4,6-dione 12

Reaction of **6** and **8** using Method 1 (*T* 35 °C; *t* 6 h) gave **12** as a beige solid (90%), mp 225.5–227.1 °C. (Found: C, 51.55; H, 4.55; N, 14.95. $C_{12}H_{13}N_3O_5$ requires C, 51.6; H, 4.7; N, 15.05%.) δ_H (d_6-DMSO) 11.40 (1H, d, ^{3}J 14.3), 8.84 (1H, d, ^{3}J 14.3), 7.96 (1H, d, ^{3}J 4.8), 7.75 (1H, d, ^{3}J 4.8), 3.74 (3H, s), and 1.69 (6H, s); δ_C (d_6-DMSO) 164.0 (quat), 161.8 (quat), 155.3 (quat), 151.6, 136.9, 135.1 (quat), 110.7, 104.9 (quat), 90.9 (quat), 39.9 (CH_3) and 26.6 ($2CH_3$); ν_{max} 3212, 1728, 1692, 1652, 1586, 1476, 1390, 1360, 1306, 1270, 1230, 1204, 1150, 1110, 1030, 998, 958, 920, 868 and 830 cm^{-1}.

5-[(5-Chloro-2-methyl-3-oxo-2,3-dihydropyridazin-4-ylamino)methylene]-2,2-dimethyl-1,3-dioxane-4,6-dione 13

Reaction of **7** and **8** using Method 1 (*T* 50 °C; *t* 4 h) gave **13** as a white solid (57%), mp 196.6–197.0 °C. (Found: C, 45.9; H, 3.6; N, 13.4. $C_{12}H_{12}ClN_3O_5$ requires C, 45.95; H, 3.85; N, 13.4.) δ_H (d_6-DMSO) 11.49 (1H, d, ^{3}J 13.4), 9.76 (1H, d, ^{3}J 13.4), 8.23 (1H, s), 3.73 (3H, s) and 1.70 (6H, s); δ_C (d_6-DMSO) 164.6 (quat), 161.8 (quat), 154.7, 154.5 (quat), 136.7, 130.8, 122.3, 105.3 (quat), 90.1 (quat), 40.3 (CH_3) and 26.6 ($2CH_3$) (2 quats not assigned); ν_{max} 3748, 3618, 3568, 3422, 3068, 3004, 2942, 1732, 1690, 1642, 1610, 1450, 1380, 1274, 1186, 1136, 1026, 972, 918 and 830 cm^{-1}.

5-[(2,6-Dichlorophenylamino)methylene]-2,2-dimethyl-1,3-dioxane-4,6-dione 14

Using Method 2, reaction of 2,6-dichloroaniline (1.62 g, 10 mmol) with **8** gave 5-[(2,6-dichlorophenylamino)methylene]-2,2-dimethyl-1,3-dioxane-4,6-dione **14** as a yellow solid (2.89 g, 91%); mp 119–120 °C (from ethanol); (Found C, 49.6; H, 3.15; N, 4.3. $C_{13}H_{11}Cl_2NO_4$ requires C, 49.4; H, 3.5; N, 4.45%); δ_H 11.05 (1H, d, ^3J 13.9), 8.55 (1H, d, ^3J 13.9), 7.45 (2H, d, ^3J 7.9), 7.08 (1H, dd, ^3J 7.7, ^4J 1.0) and 1.79 (6H, s); δ_C 165.2 (quat), 162.9 (quat), 158.2, 133.2 (quat), 129.5 (2 quat), 129.3 (2CH), 128.5, 105.2 (quat), 88.0 (quat) and 27.0 ($2CH_3$); *m*/*z* 317 (M^+, 11%), 315 (M^+, 16), 259 (59), 257 (89), 180 (42) and 178 (100).

5-[(4-Chloro-2-formylphenylamino)methylene]-2,2-dimethyl-1,3-dioxane-4,6-dione 15

Using Method 2, a solution of 2-amino-5-chlorobenzaldehyde (0.502 g, 3.24 mmol) in acetonitrile (40 cm^3) was treated with a solution of **8** (0.596 g, 3.20 mmol) in acetonitrile (4 cm^3) and the mixture was stirred at room temperature for 1 h. The resulting precipitate was collected and washed with acetonitrile to yield 5-[(4-chloro-2-formylphenylamino)methylene]-2,2-dimethyl-1,3-dioxane-4,6-dione **15** (0.644 g, 65%); mp 225–227 °C; (Found: C, 54.25; H, 3.8; N, 4.5. $C_{14}H_{12}ClNO_5$ requires C, 54.3; H, 3.9; N, 4.5%); δ_H (d_6-DMSO) 13.02 (1H, br d, *J* 14.0, NH), 10.00 (1H, s, aldehyde), 8.80 (1H, d, ^3J 14.0, alkene), 8.14 [1H, d, $^4J_{3,5}$ 2.5, H(3)], 8.00 [1H, d, $^3J_{5,6}$ 9.0, H(6)], 7.82 [1H, dd, $^3J_{5,6}$ 9.0 and $^4J_{3,5}$ 2.5, H(5)] and 1.72 (6H, s, $2CH_3$); δ_C (d_6-DMSO) 193.9, 163.0 (quat), 162.3 (quat), 151.1, 127.1 (quat), 135.1, 135.0, 129.3 (quat), 124.4 (quat), 118.6, 104.2 (quat), 89.2 (quat) and 26.4 ($2CH_3$); *m*/*z* 309 (M^+, 5%), 209 (32), 207 (100), 162 (39), 99 (24) and 75 (28).

3-[(2,2-Dimethyl-4,6-dioxo-1,3-dioxan-5-ylidenemethyl)amino]thiophene-2-carbaldehyde 16

Using Method 2, a solution of 3-aminothiophene-2-carboxaldehyde (200 mg, 1.5 mmol) (ESI†) in acetonitrile (5 cm^3) was treated with a solution of **8** (260 mg, 1.5 mmol) in acetonitrile (2 cm^3) and the mixture was stirred at room temperature for 30 min. The resulting precipitate was collected and washed with acetonitrile to yield 3-[(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidenemethyl)amino]thiophene-2-carbaldehyde **16** (114 mg, 27%); mp 218–220 °C; (Found: M^+ 218.0358. $C_{12}H_{11}NO_5$ requires *M* 281.0358); δ_H 12.85 (1H, br d, ^3J 14.0, NH), 9.83 (1H, s, aldehyde), 8.62 (1H, d, ^3J 14.0, alkene), 7.80 (1H, d, ^3J 5.3, thiophene-H), 7.36 (1H, d, ^3J 5.3, thiophene-H) and 1.74 (6H, s, $2CH_3$); δ_C 183.2 (quat), 164.1 (quat), 163.8 (quat), 152.1, 143.4 (quat), 136.5, 123.8 (quat), 118.1, 105.7 (quat), 90.0 (quat) and 27.6 ($2CH_3$); *m*/*z* 281 (M^+, 7%), 223 (42), 151 (46), 85 (65), 71 (77) and 57 (100).

FVP reactions

FVP experiments were carried out by sublimation/distillation of the substrate *in vacuo* through an electrically heated silica furnace tube (35 × 2.5 cm). Products were trapped in a U-tube situated at the exit point of the furnace and cooled with liquid nitrogen. Pyrolysis conditions are quoted as follows: substrate, quantity, furnace temperature (T_f), inlet temperature (T_i), pressure (range if appropriate) (*P*), pyrolysis time (*t*) and products.

FVP of 2,2-dimethyl-5-[(1-methyl-6-oxo-1,6-dihydropyridazin-4-ylamino)methylene]-1,3-dioxane-4,6-dione 9

FVP of compound **9** (0.1035 g, T_f 600 °C, T_i 210 °C, *P* 2.5–2.7 × 10^{-2} Torr, *t* 30 min) gave 4-hydroxy-6-methyl-6*H*-pyrido[2,3-*d*]-pyridazin-5-one **17** as a pale yellow solid (0.0459 g, 70%); mp 244–246 °C; (Found M^+ 177.05350. $C_8H_7N_3O_2$ requires *M* 177.05328); δ_H (360 MHz, d_6-DMSO, 80 °C) 8.42 (1H, s, br), 8.23 (1H, s, br), 7.09 (1H, s, br) and 3.77 (3H, s); addition of TFA to the DMSO sample sharpened the signals to give the following spectrum: δ_H (d_6-DMSO + TFA) 8.77 (1H, d, ^3J 5.9), 8.49 (1H, s), 7.15 (1H, d, ^3J 5.9) and 3.74 (3H, s); *m*/*z* 177 (M^+, 100%), 149 (37), 121 (11) and 106 (13).

FVP of 5-[(5-chloro-1-methyl-6-oxo-1,6-dihydropyridazin-4-ylamino)methylene]-2,2-dimethyl-1,3-dioxane-4,6-dione 10

FVP of **10** (0.116 g, T_f 600 °C, T_i 210 °C, *P* 2.3–2.6 × 10^{-2} Torr, *t* 45 min) gave 3-chloro-4-hydroxy-6-methyl-6*H*-pyrido[2,3-*d*]pyridazin-5-one **18** as a yellow-white solid (0.0640 g, 85%); mp 302–304 °C (decomp.); (Found M^+ 211.01445. $C_8H_6{}^{35}ClN_3O_2$ requires *M* 211.01431); NMR data could not be acquired due to insolubility (even in d_6-DMSO) so the product was characterised by its mass spectrum; *m*/*z* 213 (M^+, 34%), 211 (M^+, 100), 177 (83), 159 (70), 136 (57) and 105 (49).

FVP of 2,2-dimethyl-5-[(1-methyl-6-oxo-3-phenyl-1,6-dihydropyridazin-4-ylamino)methylene]-1,3-dioxane-4,6-dione 11

FVP of **11** (0.250 g, T_f 600 °C, T_i 200 °C, *P* 2.3 × 10^{-2} Torr, *t* 35 min) gave 4-hydroxy-6-methyl-8-phenyl-6*H*-pyrido[2,3-*d*]pyridazin-5-one **19** as an off-white solid (0.141 g, 96%); mp 163–165 °C; (Found M^+ 253.08459. $C_{14}H_{11}N_3O_2$ requires *M* 253.08458); δ_H (d_6-DMSO) 8.87 (1H, d, ^3J 5.3), 8.01–7.92 (2H, m), 7.55–7.51 (3H, m), 7.26 (1H, d, ^3J 5.3) and 3.87 (3H, s); δ_C (d_6-DMSO) 166.2 (quat), 162.5 (quat), 156.9, 147.6 (quat), 146.3 (quat), 134.0 (quat), 130.1 (2CH), 129.2, 127.8 (2CH), 112.1, 111.6 (quat) and 38.7 (CH_3); *m*/*z* 253 (M^+, 100%) and 252 (62).

4-Hydroxy-6-methyl-8-phenyl-6*H*-pyrido[2,3-*d*]pyridazin-5-one 19

The microwave-assisted heating of **11** (200 mg, 0.8 mmol) at 165 °C for 50 min gave, after purification by column chromatography (silica, eluent: dichloromethane), 4-hydroxy-6-methyl-8-phenyl-6*H*-pyrido[2,3-*d*]pyridazin-5-one **19** (89 mg, 62%) as a white solid, mp 169.0–169.6 °C. (Found: C, 66.35; H, 4.0; N, 16.55. $C_{14}H_{11}N_3O_2$ (253.26) requires C, 66.4; H, 4.4; N, 16.6%.) δ_H ($CDCl_3$, 600 MHz) 13.02 (1H, s), 8.80 (1H, d, ^3J 5.5), 7.91 (2H, d, ^3J 5.6), 7.53–7.47 (3H, m), 7.04 (1H, d, ^3J 5.5) and 3.92 (3H, s); δ_C (d_6-DMSO, 150 MHz) 167.9 (quat), 163.7 (quat), 157.4, 149.5 (quat), 147.5 (quat), 134.5 (quat), 130.7 (2CH), 130.3, 128.9 (2CH), 112.9, 112.7 (quat) and 39.6 (CH_3).

FVP of 2,2-dimethyl-5-[(2-methyl-3-oxo-2,3-dihydropyridazin-4-ylamino)methylene]-1,3-dioxane-4,6-dione 12

FVP of **12** (0.1033 g, T_f 600 °C, T_i 190 °C, P 2.2–2.3 × 10^{-2} Torr, t 45 min) gave two products, a white solid formed at the exit point of the furnace and a yellow solid formed at the liquid nitrogen level of the trap. The insoluble white solid was suspended in acetone, and removed from the U-tube. Removal of the acetone gave 7-methyl-1,7-dihydropyrido[2,3-*d*]pyridazine-4,8-dione **22** (0.0127 g, 19%) as a white solid, mp >310 °C; (Found M^+ 177.05318. $C_8H_7N_3O_2$ requires M 177.05328); δ_H (360 MHz, d_6-DMSO) 8.32 (1H, s), 7.90 (1H, d, ^3J 7.5), 6.44 (1H, d, ^3J 7.5) and 3.79 (3H, s); δ_C (90 MHz, d_6-DMSO) 175.3 (quat), 155.2 (quat), 140.2, 136.3 (quat), 133.5, 119.8, 117.6 (quat) and 39.4 (CH_3); m/z 177 (M^+, 13%), 159 (27), 136 (100), 120 (12), 105 (91) and 91 (45).

The yellow solid was dissolved in dichloromethane and the solution removed from the U-tube; concentration of the solution gave 1-methyl-1*H*-pyrrolo[3,2-*c*]pyridazine **24** (0.0308 g, 63%) as a brown-yellow solid mp 64–66 °C; (Found M^+ 133.06353. $C_7H_7N_3$ requires M 133.06345); δ_H (360 MHz) 8.47 (1H, d, ^3J 2.2), 8.39 (1H, d, ^3J 5.4), 7.90 (1H, dd, ^3J 5.4, ^4J 0.9), 6.52 (1H, dd, ^3J 2.2, ^4J 0.9) and 4.42 (3H, s); δ_C (90 MHz) 158.3, 148.0 (quat), 144.9 (quat), 136.4, 116.8, 91.3 and 46.2 (CH_3); m/z 133 (M^+, 14%), 91 (14), 75 (14), 66 (59) and 52 (100).

FVP of 5-[(5-chloro-2-methyl-3-oxo-2,3-dihydropyridazin-4-yl-amino)methylene]-2,2-dimethyl-1,3-dioxane-4,6-dione 13

FVP of **13** (0.252 g, T_f 600 °C, T_i 200 °C, P 2.8–3.0 × 10^{-2} Torr, t 11 min) gave a white solid condensate at the exit point of the furnace and yellow solid deeper in the U-tube trap. The entire pyrolysate was washed from the trap with methanol, and the insoluble white solid filtered off to give 3-chloro-7-methyl-1,7-dihydropyrido[2,3-*d*]pyridazine-4,8-dione **23** (0.0573 g, 34%), mp >310 °C; (Found M^+ 211.01416. $C_8H_6{}^{35}ClN_3O_2$ requires M 211.01431) δ_H (360 MHz, d_6-DMSO) 13.01 (1H, br s), 8.37 (1H, s), 8.31 (1H, s) and 3.79 (3H, s); δ_C (90 MHz, d_6-DMSO) 169.7 (quat), 155.0 (quat), 138.6, 135.4 (quat), 133.8, 123.6 (quat) and 39.5 (CH_3) (one quaternary signal not apparent); m/z 213 (M^+, 33%), 211 (M^+, 100), 183 (53), 159 (66) and 135 (72).

The methanolic solution was absorbed onto alumina and column chromatography (ethyl acetate) gave 4-chloro-1-methyl-1*H*-pyrrolo[3,2-*c*]pyridazine **25** as an orange solid (0.0214 g, 16%), mp 55–57 °C; (Found M^+ 167.02473. $C_7H_6{}^{35}ClN_3$ requires M 167.02448); δ_H 8.43 (1H, d, ^3J 2.0), 8.35 (1H, s), 6.53 (1H, d, ^3J 2.0) and 4.51 (3H, s); δ_C 158.1, 144.8 (quat), 136.1, 126.2 (quat), 105.4 (quat), 98.9 and 46.0 (CH_3); m/z 169 (M^+, 30%), 167 (M^+, 100) and 104 (13).

3,8-Dichloroquinolin-4(1*H*)-one 21

FVP of **14** (0.354 g, T_f 600 °C, T_i 190 °C, P 2.5–3.0 × 10^{-2} Torr, t 15 min) gave a yellow-brown solid. Minor soluble impurities were removed by distillation of dichloromethane through the U-tube. Suspension of the residual solid in acetone and removal of the solvent gave 3,8-dichloroquinolin-4-one **21** as a brown solid (0.128 g, 54%), mp 255–257 °C (decomp.); (Found M^+ 212.97454, $C_9H_5{}^{35}Cl_2NO$ requires M 212.97427); δ_H (d_6-DMSO) 11.94 (1H, br, s), 8.25 (1H, br, m), 8.18 (1H, dd, ^3J 8.3, ^4J 1.5), 7.93 (1H, dd, ^3J 7.8, ^4J 1.5) and 7.44 (1H, dd, ^3J 8.3, ^3J 7.8); δ_C (d_6-DMSO) 170.9 (quat), 138.3, 135.7 (quat), 132.1, 125.9 (quat), 124.7, 124.6, 121.9 (quat) and 115.2 (quat); m/z 215 (M^+, 35%), 213 (M^+, 53), 163 (85), 161 (100) and 84 (85).

6-Chloroquinoline 30

The pyrolysate from FVP of **15** (288 mg, T_f 550 °C, T_i 220 °C, P 1.0 × 10^{-2} Torr, t 14 min) was washed through with dichloromethane and the solvent removed to yield 6-chloroquinoline **30** (95 mg, 62%); δ_H 8.92 [1H, dd, $^3J_{4,3}$ 4.3 and $^4J_{4,2}$ 1.6, H(4)], 8.03–8.12 [(2H, m, H(2) and H(8)], 7.81 [1H, d, $^4J_{5,7}$ 2.3, H(5)], 7.65 [1H, dd, $^3J_{7,8}$ 9.0, $^4J_{7,5}$ 2.3, H(7)] and 7.44 [1H, dd, $^3J_{3,4}$ 4.3 and $^3J_{3,2}$ 8.2, H(3)], consistent with reported data;[22] δ_C 150.3, 146.3 (quat), 135.2, 132.3 (quat), 130.8, 130.4, 128.7 (quat), 126.3 and 121.8; m/z 165 (M^+, 34%), 163 (M^+, 100), 128 (30), 101 (11) and 75 (15).

FVP of 3-[(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidenemethyl)-amino]thiophene-2-carbaldehyde 16

FVP of **16** (21 mg, T_f 550 °C, T_i 120 °C, P 2.1 × 10^{-2} Torr, t 8 min) yielded thieno[3,2-*b*]pyridine **31** and 4*H*-thieno[3,2-*b*]-pyridin-7-one **32** in a ratio of 1 : 1 (identified by ^{1}H NMR spectroscopy).

FVP of **16** (21 mg, T_f 850 °C, T_i 130 °C, P 2.3 × 10^{-2} Torr, t 7 min) yielded thieno[3,2-*b*]pyridine **31** and 4*H*-thieno[3,2-*b*]pyridin-7(4*H*)-one **32** in a ratio of 2 : 1. Spectral data for **32**: δ_H (d_6-DMSO) 7.99 (1H, d, ^3J 5.5, thiophene-H), 7.87 (1H, d, ^3J 7.2, pyridone-H), 7.27 (1H, d, ^3J 5.5, thiophene-H) and 6.07 (1H, d, ^3J 7.2, pyridone-H) consistent with literature data;[23] δ_C (d_6-DMSO) 173.5 (quat), 166.9 (quat), 137.9 (quat), 113.4 (2CH), 118.9 and 109.6; m/z 151 (M^+, 100%), 135 (48), 134 (49), 125 (29), 96 (33) and 69 (48).

The pyrolysate obtained by FVP of **16** (61 mg, T_f 850 °C, T_i 120 °C, P 2.1 × 10^{-2} Torr, t 10 min) was washed from the U-tube with warm $CDCl_3$ (1 cm^3) to yield thieno[3,2-*b*]-pyridine **31** (17 mg, 57%); bp 145 °C (42 Torr) [lit.,[24] 129–131 °C (16 Torr)]; δ_H 8.68 [1H, dd, $^3J_{5,6}$ 4.7 and $^4J_{5,7}$ 1.5, H(5)], 8.19 [1H, ddd, $^3J_{7,6}$ 8.2 $^4J_{7,5}$ 1.5 and ^nJ 0.9, H(7)], 7.76 (1H, dd, ^3J 5.6 and ^nJ 0.4, thiophene-H), 7.57 (1H, dd, ^3J 5.6 and ^nJ 0.9, thiophene-H) and 7.25 [1H, ddd, $^3J_{6,5}$ 4.7, $^3J_{7,6}$ 8.2 and ^nJ 0.4, H(6)]; δ_C 156.1 (quat), 147.4, 133.4 (quat), 130.8, 130.7, 125.3 and 118.8; m/z 135 (M^+, 100%), 134 (33), 112 (20), 99 (20), 73 (29) and 69 (33).

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