Mesoions and ketene valence isomers. Pyrrolo[1,2-*a*]pyridinylium olates and (2-pyridyl)carbonylketenes †

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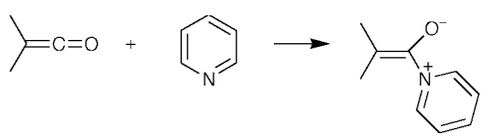
Received (in Cambridge, UK) 23rd August 1999, Accepted 15th November 1999

The zwitterionic title compounds **5a–d** are obtained by FVT of picolinoylacetates **3a–d**. Compounds **5a–d** undergo nucleophilic addition reactions by C–N bond cleavage to afford pyridine derivatives **6–12**. The thermal and photochemical ring opening of **5a** to the ketene valence isomer **4a** is demonstrated by matrix isolation IR spectroscopy and supported by excellent agreement with DFT calculations.

Introduction

We have demonstrated in previous work that reactions between ketenes and nucleophiles, pyridine in particular, take place at extremely low temperatures (15–40 K), to generate ketene-pyridine zwitterions **1**.[1]



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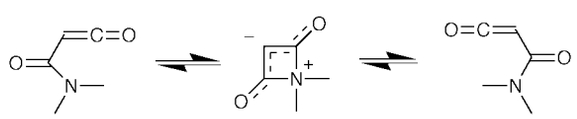

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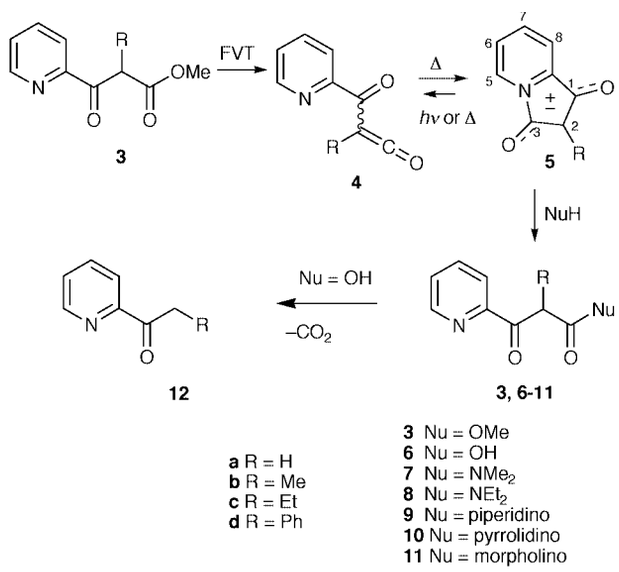
The kinetic monitoring of such reactions revealed that they have extremely low activation enthalpies (order of 1 kJ mol^{-1}) and very large and negative activation entropies (order of −300 J K^{-1} mol^{-1}).[1a,b]

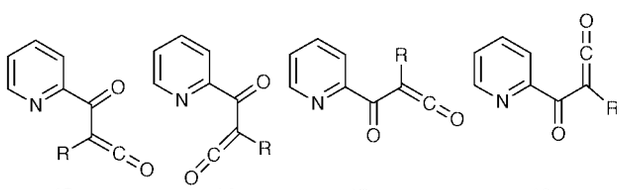
Intramolecular interaction between an amine substituent and a ketene is indicated in the facile 1,3-shift of (dimethyl)-amino groups in acylketenes, which has a very low calculated activation barrier (*ca.* 34 kJ mol^{-1}; *ca.* 8 kcal mol^{-1}).[2] The zwitterionic intermediate **2** is predicted to exist in a shallow minimum, but no such species has ever been observed.

We reasoned that such zwitterions could be made more stable, and thus observable, by incorporating them in five-membered rather than four-membered rings. Other examples of intramolecular ketene-amine zwitterions have been described, but here the valence isomeric ketenes have never been observed.[3,4] Here, we report the successful generation and isolation of the pyrrolopyridinium olate system **5**, direct spectroscopic evidence for its ring opening to the valence isomeric ketenes **4**, some of the chemical reactions of **5**, and theoretical calculations supporting the IR spectroscopic identification and relating to the energy profile of the mesoion–ketene system.

† Calculated structures and energies, and Cartesian coordinates for compounds **5** and **13–16**, as well as transition state energies for the interconversions between **4a**,**5a** and **13–16a**, and calculated ^{13}C NMR data for **5a** are available as supplementary data. For direct electronic access see http://www.rsc.org/suppdata/p1/a9/a906831g.



3 **4** **5** **12** **3, 6-11**



13 **14** **15** **16**

Scheme 1

Results and discussion

Flash vacuum thermolysis (FVT) of the 2-picolinylacetates **3** at 550 °C gave rise to red-to-purple solids, which were stable at room temperature in the absence of nucleophiles. **5a** in particular is extremely sensitive to moisture. The substituted derivatives **5b–d** are significantly less sensitive. The spectroscopic properties of these compounds are summarised in Tables 1 and 2. In the NMR spectra, it is seen that 2-C appears at relatively high fields (79–91 ppm) and this is also the case for 2-H and 2-alkyl groups as well as the "ketone" and "lactam" carbonyl carbons 1-C and 3-C, in agreement with the presence of a negative charge over the C1–C3 fragment. The relatively weak (1/5 to 1/9 of the intensities of other CH signals) and broad (FWHH ~15 Hz at 100.6 MHz) signal for 5-C at δ ^{13}C = 131–133 ppm is also notable. The broadness can be ascribed to the

Table 1 ^{13}C and ^{1}H NMR data for **5**[a]

Cpd	R	C_5–H_5	C_6–H_6	C_7–H_7	C_8–H_8	C_{8a}	C_2–(H_2)	C_3 and C_1	CH_3, CH_2 or C (Ph)	CH_3, CH_2 or *Ph*
5a	H	131.0–8.70	126.8–7.90	148.0–7.91	117.2–7.90	143.9	78.8–4.8	165.7, 180.9		
5b	Me	132.2–8.81	127.5–7.96	149.1–8.55	115.9–7.76	141.2	84.8–—	165.6, 179.7	5.61	1.63 CH_3
5c	Et	132.3–8.80	127.6–7.97	149.2–8.55	116.0–7.75	141.7	91.2–—	165.2, 179.1	13.5, 14.2	1.01, 2.13 CH_3CH_2
5d	Ph	132.6–8.80	128.2–7.99	149.9–8.57	116.9–7.85	141.5	89.3–—	164.4, 178.4	124.1 (*o*), 124.1 (*p*), 127.9 (*m*), 133.2 (C_1)	7.04 (*p*), 7.27 (*m*), 8.16 (*o*)

[a] 400/100.6 MHz, DMSO-d_6. ^{13}C–^{1}H correlations by COSY.

Table 2 UV, IR and MS data for compounds **5a**–**d**[a]

							MS *m*/*z* (rel. abundance)			
Cpd	R	λ_{max}/nm	log (ε/dm^3 mol^{-1} cm^{-1})	λ_{max}/nm	log (ε/dm^3 mol^{-1} cm^{-1})	IR ($\nu_{C=O}$)/ cm^{-1}	$M^{+\bullet}$	*m*/*z* 78 $(C_5H_4N)^{+\bullet}$	RC(CO)CO$^{+\bullet}$ $(M - 78)^{+\bullet}$	RCCO$^{+\bullet}$ $(M - 78 - CO)^{+\bullet}$
5a	H	233	3.65	450	2.95	1743, 1653	147 (65)	(100)	69 (72)	41 (30)
5b	Me	229	4.11	498	2.92	1746, 1654	161 (80)	(100)	83 (31)	55 (13)
5c	Et	237	3.75	501	2.83	1740, 1645	175 (43)	(74)	—[b]	69 (13)
5d	Ph	273	3.98	538	2.67	1734, 1644	223 (100)	(76)	145 (4)	117 (6)

[a] UV spectra in CH_2Cl_2; IR spectra in KBr; MS at 70 eV EI. [b] *m*/*z* 160 (M − 15) = 100% formed instead.

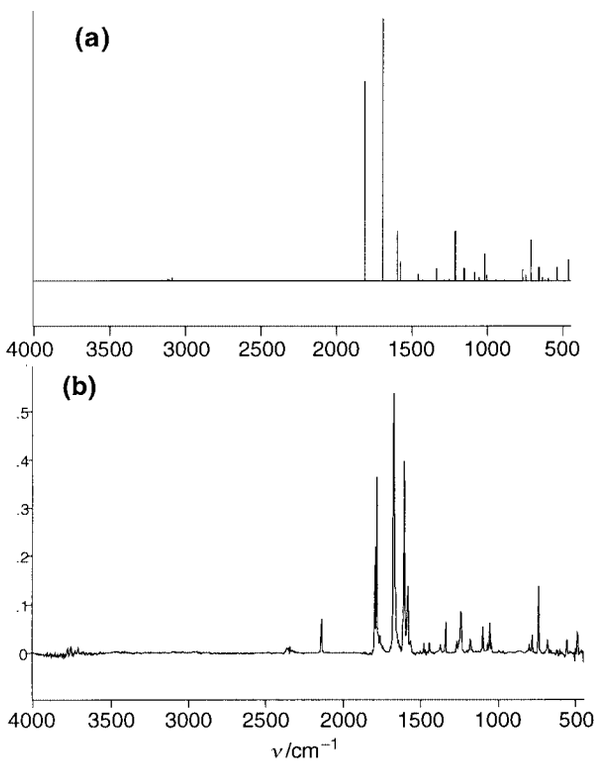


Fig. 1 IR spectrum of compound **5a**, (a) calculated at the B3LYP/6-31G* level (ε = 40; frequencies scaled by 0.9613); (b) obtained after deposition in argon matrix (7 K). The band at 2142 cm^{-1} is assigned to the ketene **4a**. See Experimental section for peak listing.

quadrupole moment of a directly attached ^{14}N nucleus.[5] Notably, the appearance of an α-CH signal (5-C in **5**) in a pyridine at such a high field (it is normally expected in the 140–150 ppm range) suggests that the pyridine nitrogen carries a positive charge, as in pyridinium compounds.[5] In agreement with this, the pyridine γ-CH (7-C) is at an unusually low field (148–150 ppm), and the quaternary α-C signal (8a-C; 144 ppm) is also very weak and broadened. Similar ^{13}C NMR characteristics are observed for other, six-membered, mesoionic compounds (pyrido-pyrimidinium and -oxazinium olates).[6] In the IR spectra, two carbonyl groups are observed, a "ketone" and a "lactam" type. The IR spectrum of **5a** is in excellent agreement with calculations (see Fig. 1 and the Theory section). All the compounds give rise to intense signals for the pyridyl ion (*m*/*z* 78) in the mass spectra, and mostly also signals corresponding to the RC(CO)CO and RCCO fragments.

Further evidence for the structures of **5** is given by their chemical reactions. Although **5a** is stable at room temperature in the solid state, it is extremely sensitive to moisture, which causes rapid formation of 2-acetylpyridine (**12a**), the product of decarboxylation of the unobserved acid **6a**. Compounds **5a**–**d** reacted with methanol and amines at room temperature to produce the picolinoylacetic acid derivatives **3** and **7**–**11**, and with water to produce **12**, in yields up to 99%.

The 2-phenyl derivative **5d** has been prepared before in an entirely different way.[4] Its structure was secured by X-ray crystal analysis,[4] and our material had spectroscopic properties identical with those reported. The reported chemistry of **5d** is very surprising, since it was said to undergo cleavage of the C8a–C1 bond rather than the expected C–N bond cleavage on reaction with nucleophiles (morpholine).[4] Nevertheless, we find that **5d** reacts just like the other derivatives (**5a**–**c**) to afford compounds **7d**–**11d**, whereby the reaction with pyrrolidine is far more rapid (5 min) than that with morpholine (23 h). The morpholine derivative **11d** decomposes if this reaction is left for too long; this may explain why it was not obtained by Potts *et al.* (10 days reaction time reported in ref. 4*a*).

Mesoion–ketene valence isomerization

Evidence for ring opening of mesoion **5a** to the acylketene valence isomer **4a** was obtained by matrix isolation. Sublimation of **5a** at 100 °C with deposition of the vapour with Ar at 7–10 K gave rise to a weak absorption at 2142 cm^{-1} ascribed to a ketene; this band is seen in the spectrum in Fig. 1b. The remaining bands in Fig. 1b are due to mesoion **5a**. This spectrum is in very good agreement with the B3LYP/6-31G* calculated IR spectrum (Fig. 1a). Photolysis of **5a** in the Ar matrix at 7–10 K caused rapid increase in the intensity of the 2142 cm^{-1} band, with concomitant decrease of the bands assigned to **5a**. The spectrum of the resulting ketene is shown in Fig. 2b and agrees very well with the calculated spectrum in Fig. 2a (see the Experimental section for a full listing of experimental and calculated data). In the frequency range below 3000 cm^{-1} all calculated bands with an intensity above 11 km mol^{-1} have an experimental counterpart. Similar experiments in a Xe matrix showed that the ketene was stable till at least 70 K, but changes due to annealing of different sites or conformers of the ketene in the matrix took place at 50–60 K. When an Ar matrix was

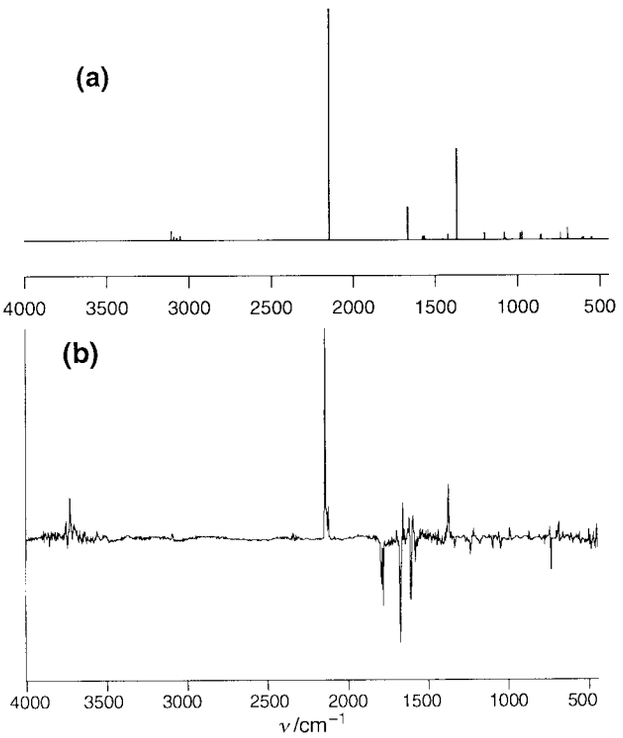


Fig. 2 IR spectrum of ketene **4a**, (a) s*E*-s*Z* conformer **13** calculated at the B3LYP/6-31G* level (gas phase); (b) difference spectrum obtained after photolysis of **5a** (Ar, 7 K, 60 min; broad band high-pressure Hg/Xe lamp, 1000 W); positive peaks are due to **4a**, negative peaks to **5a**. See Experimental section for peak listing.

allowed to evaporate above 40 K, the remaining neat ketene disappeared on subsequent warm-up to 150 K.

Compounds **5b–d** were examined in a similar manner, and it was found that these are far less prone to ring opening to ketenes than is the parent compound **5a**. Matrix deposition of **5b–d** by sublimation at *ca.* 100 °C in a stream of Ar gave rise to very weak absorptions in the ketene region. Matrix deposition through the FVT tube at 700 °C gave ketene signals that were significantly stronger but still weak, similar to the result in Fig. 1b. Subsequent photolysis under a variety of conditions did not result in large increases in the intensities of the ketene bands. This may be understood in terms of the calculations reported below, according to which the conformers **14**, which would form initially on photolysis, are not stable but undergo barrier-free ring closure to **5**. Thus, only the rotamers **13**, **15**, or **16** would be observable in the matrix. The substituents R would make rotation of the ketene moieties difficult in the rigid matrices. Moreover, the ring-closed forms **5** are found computationally to be relatively more stable than the ketenes **13** in the substituted cases. Accordingly, the activation barriers for ring opening of substituted **5** are significantly higher than for the unsubstituted **5a**.

Theory

DFT calculations[7] of the structure and IR spectrum of mesoion **5a** at the B3LYP/6-31G* level[8] indicate a long ylidic N(4)–C(3) bond (1.601 Å for the gas phase, relative permittivity $\varepsilon = 1$). This is shortened to 1.575 Å for $\varepsilon = 40$ (simulating a polar environment).[9] The stretching frequency of the ylidic C=O "lactam" group C3 in the IR spectrum is correspondingly high: 1814 cm^{-1} for the gas phase calculation and 1794 cm^{-1} for $\varepsilon = 40$. The experimental value is 1794/1783 cm^{-1} (two sites). The "normal" ketone C=O vibration of C1 is calculated as 1693 (gas phase) or 1681 cm^{-1} ($\varepsilon = 40$). The experimental value is 1676 cm^{-1}. There is very good overall agreement between the experimental matrix IR spectrum and the calculated one for $\varepsilon = 40$ (Fig. 1). The shortening of the zwitterionic N–CO bond and the decrease in the C=O stretching frequency on increasing the polarity of the medium are in accord with similar observations made on intermolecular ketene-pyridine zwitterions.[1b] It is also seen that the C=O stretching frequencies of the solids in KBr (Table 2) are very much lower than for the Ar matrices. This, too, is in accord with observations made on other, six-membered mesoionic compounds, *viz*. pyridopyrimidinium and pyridooxazinium olates.[6]

For **5b** and **5d** the calculated zwitterionic N(4)–C(3) bond lengths are 1.592 and 1.562 ($\varepsilon = 1$), or 1.564 and 1.530 Å ($\varepsilon = 40$), respectively. The latter number can be compared with the experimental value from the X-ray structure of **5d**: 1.516(3) Å.[4a] Thus, structural parameters and infrared spectra indicate that good agreement with experiment is obtained for mesoionic compounds **5** provided a highly polar environment is taken into account. The calculated structures of **5a**, **5b**, and **5d** are presented in the Supplementary material.

Energies of ketene conformers and the barriers for the various possible interconversions between them and **5a** were calculated at the B3LYP/6-311+G(3df,2p)//B3LYP/6-31G* + ZPVE level. The structures and relative energies are presented in the Supplementary material. The lowest energy conformations of ketene **4a** are **13a** with s*E*-s*Z* configuration, and **14a** with s*E*-s*E* configuration of the N=C–(C=O)–C=C=O moiety. The gas phase ring opening of mesoion **5a** to **13a** has a calculated activation barrier of 73 kJ mol^{-1} (17 kcal mol^{-1}) and is endothermic by 17 kJ mol^{-1} (4 kcal mol^{-1}). These values increase to 93 and 42 kJ mol^{-1}, respectively, in a polar medium ($\varepsilon = 40$). The s*E*-s*E* ketene **14a** is calculated to lie only 8 kJ mol^{-1} above **5a**, and the transition structure between the two lies 9 kJ mol^{-1} above **5a**. In the polar medium ($\varepsilon = 40$), **14a** collapses without a barrier to mesoion **5a**. Therefore, ketene **14a** would not be stable under our matrix isolation conditions. Methyl substitution leads to increased relative stability of the mesoion **5b**, which is now more stable than the most stable ketene form **13b** by 47 kJ mol^{-1} (gas phase; 72 kJ mol^{-1} for $\varepsilon = 40$). The ring opening of **5b** is predicted to have an energy barrier of 85 kJ mol^{-1} (gas phase; 102 kJ mol^{-1} for $\varepsilon = 40$).

Two other conformers of ketene **4a** exist, namely **15a** (s*Z*-s*Z*) and **16a** (s*Z*-s*E*), which are both calculated to lie 50 kJ mol^{-1} above **5a** (gas phase values; these increase to 61 and 63 kJ mol^{-1}, respectively, for $\varepsilon = 40$).

Conclusion

Spectroscopy, calculations and chemistry agree in the identification of mesoion **5a** and its ketene valence isomer **4a** (as conformer **13a**). This is one of the very few cases[10] where such valence isomerisation of five-membered mesoions has been established. Analogous ring opening of sydnones and münchnones to ketenes has been much discussed, but no concrete evidence has been presented.[11]

Experimental

General

Infrared spectra were recorded on Perkin-Elmer 1700X or System 2000 FTIR spectrometers. UV spectra were measured on Shimadzu UV-160 or Varian Cary 1 spectrometers. Mass spectra were obtained using a Kratos MS25RFA spectrometer (direct insertion with electron ionization at 70 eV). NMR spectra were recorded on Bruker AC200 (200 MHz for ^1H and 50 MHz for ^{13}C) or Bruker AM400 spectrometers (400 MHz for ^1H and 100.6 MHz for ^{13}C). *J* values are given in Hz. Preparative flash vacuum thermolysis (FVT) experiments were performed using electrically heated quartz tubes (length 40 cm, diameter 2 cm). Samples were sublimed or distilled into the pyrolysis tube using a Büchi sublimation oven. The system was

evacuated to *ca.* 10^{-5} mbar and continuously pumped during the pyrolysis using a Leybold-Heraeus turbomolecular pump, PT150. Matrix isolation experiments were carried out using Leybold-Heraeus ROK 10-300 or Air Products CSW-2002-6.5K closed cycle He cryostats with BaF_2 or KBr windows. The latter cryostat was equipped with a Lakeshore Model 330 temperature controller. Samples were deposited on the cold window with a large excess of Ar (99.999%, Linde Gases). FVT with matrix isolation was performed using quartz tubes (10 × 0.8 cm i.d.) with Ar passing over the sample and through the tube. Photolyses were carried out with a 1000 W Hanovia Hg/Xe lamp.

Materials

All solvents were dried and distilled, and all liquid reagents were distilled before use. Methyl 2-picolinoylacetate[12] (**3a**) was synthesised from methyl 2-picolinate,[13] methyl acetate and NaH according to the literature. Esters **3b**–**d** were similarly prepared from methyl 2-picolinate, the appropriate ester and NaH.

Methyl 2-methyl-3-oxo-3-(2-pyridyl)propionate (3b). Sodium hydride (1.90 g; 0.05 mol) in mineral oil was washed with hexane (3 × 20 ml), and 5.0 g (0.036 mol) of methyl 2-picolinate was added under N_2. The mixture was cooled to 0 °C in a water–ice bath, and 5.07 g (0.057 mol) of methyl propionate was added dropwise over a period of 15 min. The mixture was stirred for another 15 min, the ice bath was removed, and the mixture was refluxed for 1.5 h, after which time 100 ml of ice–water was added. The resulting solution was extracted with 3 × 100 ml of diethyl ether. The organic layer was washed with saturated NaCl solution and dried over anhydrous $MgSO_4$ overnight. After filtration and evaporation of the solvent, 5.1 g of a yellow oil was collected. This was vacuum distilled to afford 4.82 g (44%) as a colourless oil (bp 92–94 °C/5 Torr); δ_H ($CDCl_3$, 200 MHz) 1.50 (d, 3H, *J* 7.2, CHC*H*$_3$), 3.67 (s, 3H, OC*H*$_3$), 4.79 (q, 1H, *J* 7.2 Hz, C*H*CH$_3$), 7.51 (m, 1H, Py-*H*$_5$), 7.87 (t, 1H, Py-H$_4$), 8.08 (d, 1H, Py-H$_3$), 8.67 (d, 1H, Py-H$_6$); δ_C ($CDCl_3$, 200 MHz) 13.2 (CH_3), 47.0 (CH_3), 52.2 (CH), 122.5 (C_3), 127.4 (C_5), 137.1 (C_4), 149.0 (C_6), 152.0 (C_2), 172.1 (C=O), 197.3 (C=O). 2D COSY ^{13}C–^{1}H correlation (400 MHz, DMSO-d_6) C_3 (122.5–8.07), C_5 (127.4–7.43), C_4 (137.1–7.80), C_6 (149.0–8.61); IR (neat) 1746, 1704, 1585 cm^{-1}; UV (CH_2Cl_2) λ_{max} 236 nm (log ε = 3.86); HRMS *m*/*z* 193.07356; calcd for $C_{10}H_{11}NO_3$ 193.073345. Anal. Calcd for $C_{10}H_{11}NO_3$ C, 62.17; H, 5.70; N, 7.25. Found C, 62.16; H, 5.74; N, 7.20%.

Methyl 2-ethyl-3-oxo-3-(2-pyridyl)propionate (3c). This was similarly obtained in 21% yield; R_f = 0.68 (hexane–$AcOCH_3$ 1 : 1); GC-MS (16 °C min^{-1}; 100–270 °C) R_t = 7.36 min; *m*/*z* 207 (M^+, 2), 160 (20), 120 (15), 106 (33), 78 (100%); UV (CH_2Cl_2) λ_{max} 246 nm (log ε = 3.34); δ_H (200 MHz, $CDCl_3$) 0.91 (t, 3H, *J* 7.4 Hz, CH_3), 1.94 (m, 2H, CH_2), 3.56 (s, 3H, OCH_3), 4.58 (t, 1H, C*H*CH$_2$), 7.40 (m, 1H, Ar-H), 7.75 (t, 1H, Ar-H), 7.96 (d, 1H, Ar-H), 8.59 (d, 1H, Ar-H); δ_C (50 MHz, $CDCl_3$) 11.9 (CH_3), 21.7 (CH_2), 51.8 (CH), 53.7 (OCH_3), 122.2 (C_3), 127.2 (C_5), 136.9 (C_4), 148.7 (C_6), 152.2 (C_2), 171.4 (C=O), 196.6 (C=O); IR 1738, 1705, 1548, 1570 cm^{-1}.

Methyl 2-phenyl-3-oxo-3-(2-pyridyl)propionate (3d). Sodium hydride (0.73 g; 15.2 mmol) was washed with hexane, and 3.04 g (22.1 mmol) of methyl 2-picolinate was added at room temperature (RT). The mixture was heated to 80 °C and 1.16 g (7.7 mmol) of methyl phenylacetate was added dropwise over a period of 10 min. The mixture was stirred for another 10 min at this temperature, causing solidification. After cooling to RT, the solid was powdered, 20 ml of benzene was added, and this mixture was refluxed for 10 min. The mixture solidified again. Water (20 ml) was added, and the resulting mixture was extracted several times with ether and dichloromethane. The combined organic phases were dried over $MgSO_4$, filtered, and the solvent evaporated. The resulting oil was purified on a column (2.5 × 45 cm; 50 g silica gel; hexane–$AcOCH_3$ 7 : 1, 460 ml) to yield 12.2%, R_f = 0.63 (hexane–$AcOCH_3$ 1 : 1), mp 99–100 °C (lit.,[14] mp 98–99 °C); GC-MS (16 °C min^{-1}; 100–270 °C) R_t = 10.9 min; *m*/*z* 255 (M^+, 36), 223 (87), 196 (14), 167 (21), 139 (3), 118 (20), 106 (51), 89 (17), 78 (100); UV (CH_2Cl_2) λ_{max} 270 (log ε = 3.47); IR (KBr) 1730, 1705, 1584 cm^{-1}; δ_H ($CDCl_3$, 200 MHz) 3.72 (s, 3H, OCH_3), 6.25 (s, 1H, CH), 7.31–7.49 (m, 6H), 7.82 (t, 1H, *J* 8 Hz, C_4-H), 8.08 (d, 1H, C_3-H, *J* 8 Hz), 8.67 (d, 1H, *J* 5 Hz, C_6-H); δ_C ($CDCl_3$, 200 MHz) 52.6 (OCH_3), 58.1 (CH), 122.8 (C_3), 127.5 (C_5), 127.9, 128.5, 129.9, 132.8 ($C_{1'}$), 137.1 (C_4), 148.9 (C_6), 151.9 (C_2), 170.0 (C=O), 194.3 (C=O).

General procedure for FVT of compounds 3a–d

The preparative pyrolyses of the esters (**3a**–**d**) were carried out at a FVT temperature of 550 °C and sublimation temperatures of 25 °C (**5a**), 50 °C (**5b**), 60 °C (**5c**), and 90 °C (**5d**). The dark red-to-purple products deposited on the cold finger at RT in yields >90% (a cold surface at RT is important in order that the coproduct methanol is not condensed). The most important spectral data for these compounds are collected in Tables 1 and 2.

2,3-Dihydro-3-oxo-1*H*-4λ^5-pyrrolo[1,2-*a*]pyridin-4-ylium-1-olate (5a). Dark red solid, mp 180 °C. HRMS *m*/*z* 147.0316; calcd for $C_8H_5NO_2$ 147.03148. Anal. Calcd for $C_8H_5NO_2$: C, 65.31; H, 3.42%. Found: C, 65.03; H, 3.33.

2,3-Dihydro-3-oxo-2-methyl-1*H*-4λ^5-pyrrolo[1,2-*a*]pyridin-4-ylium-1-olate (5b). Red-orange solid, mp 268 °C (decomp.); HRMS *m*/*z* 161.04745; calcd for $C_9H_7NO_2$ 161.04723.

2,3-Dihydro-3-oxo-2-ethyl-1*H*-4λ^5-pyrrolo[1,2-*a*]pyridin-4-ylium-1-olate (5c). Dark red solid, mp 196–198 °C; HRMS *m*/*z* 175.06301; calcd for $C_{10}H_9NO_2$ 175.06278.

2,3-Dihydro-1-hydroxy-3-oxo-2-phenyl-1*H*-4λ^5-pyrrolo[1,2-*a*]-pyridin-4-ylium-1-olate (5d). Purple solid, mp 265–268 °C (lit.,[4] 264–268 °C); HRMS *m*/*z* 223.06320; calcd for $C_{14}H_9NO_2$ 223.06278.

General procedure for reaction of mesoions 5 with nucleophiles. The requisite anhydro-1-hydroxy-3-oxo-2-R-pyrrolo-[1,2-*a*]pyridin-4-ylium hydroxide (10–100 mg) was treated with an excess of the nucleophile (methanol or amine) at RT, and the mixture was stirred at RT under N_2 for 48 h or as specified. Excess amine or methanol was evaporated, or the mixture was taken up in ether and washed with water and saturated NaCl solution, dried over $MgSO_4$, filtered and evaporated. If necessary, the crude material was purified by column chromatography. Purities were always ascertained by GC-MS and NMR spectroscopy and were >95%. The ester **3a** exists in $CDCl_3$ solution as a *ca.* 12 : 1 mixture of keto and enol forms. This compound was obtained in 98% yield by reaction of **5a** with methanol for 4 h. The amides described below can also exist as mixtures of keto and enol forms, as has been found for other, similar, amides and esters.[12,15] NMR data are given for both forms for **8a** and **9a**; for other compounds only the data for the keto forms are given, and equilibration of keto and enol forms was not attempted.

N*,*N*-Diethyl-3-oxo-3-(2-pyridyl)propionamide (8a).** To the red solution of 30 mg of **5a** in 5 ml of dry dichloromethane were added 10 drops of distilled diethylamine at RT. The colour changed immediately to brown. The NMR data indicate the formation of the keto form **8a** in equilibrium with the corresponding enol in a ratio of 1 : 2. *Data for* ***keto form: δ_H ($CDCl_3$, 400 MHz) 8.61 (br d, ^3J 4.7, 1 H), 8.03 (d, ^3J 7.8, 1 H), 7.80 (dt,

^3J 7.8, ^4J 1.7, 1 H), 7.44–7.42 (m, 1H), 4.23 (s, 2 H), 3.35 (app sextet (2 overlapping quartets), ^3J 7.1, 4 H), 1.34 (t, ^3J 7.1, 6 H); δ_C ($CDCl_3$, 100 MHz) 196.0 (C=O), 167.1 (C-1), 152.9 (C), 148.9 (CH), 136.9 (CH), 127.2 (CH), 122.0 (CH), 47.2 (C-2), 42.3 (NCH_2), 40.4 (NCH_2), 14.4 (CH_3), 13.2 (CH_3); *data for* ***enol form***: δ_H 8.57 (br d, ^3J 4.7, 1 H), 7.91 (d, ^3J 7.8, 1 H), 7.74 (dt, ^3J 7.8, ^4J 1.8, 1 H), 7.29–7.26 (m, 1H), 6.47 (s, 1 H), 3.44 (q, ^3J 7.0, 4 H), 1.24 (t, ^3J 7.0, 6 H); δ_C (400 MHz, $CDCl_3$) 171.5 (C-3), 168.6 (C-1), 152.4 (C), 149.0 (CH), 136.8 (CH), 124.7 (CH), 120.8 (CH), 86.3 (C-2), 42.8 (NCH_2), 40.1 (NCH_2), 14.2 (CH_3), 12.9 (CH_3); MS *m*/*z* 220 (M^+, 10), 202 (16), 148 (21), 121 (24), 106 (53), 93 (19), 79 (15), 78 (50), 72 (100), 58 (14); HRMS *m*/*z* 220.1208; calcd for $C_{12}H_{16}N_2O_2$ 220.1206.

The analogous product with piperidine existed as a *ca.* 1 : 1 mixture of the keto and enol forms of **9a**. *Data for* ***keto form***: δ_H (400 MHz, $CDCl_3$) 8.60 (app d, ^3J 4.6, 1 H), 8.00 (d, ^3J 7.9, 1 H), 7.78 (br t, ^3J 7.8, 1 H), 7.43–7.40 (m, 1H), 4.26 (s, 2 H); *data for* ***enol form***: δ_H 8.54 (br d, ^3J 4.6, 1 H), 7.88 (d, ^3J 7.9, 1 H), 7.72 (br t, ^3J 7.8, 1 H), 7.27–7.24 (m, 1H), 6.54; *data assigned to* ***either keto or enol form***: δ_H 3.56–3.52 (m, 6 H), 3.36–3.34 (m, 2 H), 1.76–1.51 (m, 12 H); HRMS *m*/*z* 232.1206; calcd for $C_{13}H_{16}N_2O_2$ 232.1216.

***N*,*N*-Dimethyl-2-methyl-3-oxo-3-(2-pyridyl)propionamide (7b).** Yield 55%; δ_H (400 MHz, $CDCl_3$) 1.44 (d, 3H, *J* 7, CH_3), 2.95 (s, 3H, CH_3), 3.22 (s, 3H, CH_3), 5.01 (q, 1H, *J* 7), 7.45 (t, 1H, *J* 6, Ar-H_5), 7.84 (t, 1H, *J* 8, Ar-H_4), 8.08 (d, 1H, *J* 8, Ar-H_3), 8.62 (d, 1H, J, Ar-H_6); δ_C (400 MHz, $CDCl_3$) 12.8 (CH_3), 35.6 (CH_3), 37.9 (CH_3), 44.7 (CH), 122.5 (C_3), 127.2 (C_5), 137.2 (C_4), 148.7 (C_6),152.4 (C_2), 172.2 (C=O), 197.6 (C=O). HRMS *m*/*z* 206.1053; calcd for $C_{11}H_{14}N_2O_2$ 206.10498.

***N*,*N*-Dimethyl-2-ethyl-3-oxo-3-(2-pyridyl)propionamide (7c).** Yield 89% (reaction for 24 h); δ_H (200 MHz, $CDCl_3$) 1.01 (t, 3H, *J* 7, CH_3), 2.02 (m, 2H, CH_2), 2.95 (s, 3H, CH_3), 3.26 (s, 3H, CH_3), 4.96 (t, 1H, *J* 7), 7.46 (td, 1H, C_5-H), 7.83 (td, 1H, C_4-H), 8.06 (dd, 1H, C_3-H), 8.63 (dd, 1H, C_6-H); δ_C (200 MHz, $CDCl_3$) 12.2 (CH_3), 21.8 (CH_2), 35.5 (CH_3), 37.8 (CH_3), 51.9 (CH), 122.2 (C_3), 127.1 (C_5), 136.9 (C_4), 148.6 (C_6), 152.4 (C_2), 170.9 (C=O), 196.9 (C=O). HRMS *m*/*z* 220.1202; calcd for $C_{12}H_{16}N_2O_2$ 220.12063.

***N*,*N*-Dimethyl-2-phenyl-3-oxo-3-(2-pyridyl)propionamide (7d).** Yield 81%; δ_H (200 MHz, $CDCl_3$) 2.93 (s, 3H, CH_3), 3.13 (s, 3H, CH_3), 6.08 (s, 1H, CH), 7.25–7.48 (m, 6H, C_5-H, phenyl-H), 7.80 (td, 1H, C_4-H), 8.08 (dd, 1H, C_3-H), 8.64 (dd, 1H, C_6-H); δ_C (200 MHz, $CDCl_3$) 35.6 (CH_3), 37.85 (CH_3), 56.9 (CH), 122.5 (C_3), 127.1 (C_5), 127.6, 128.5, 129.9, 133.4, 137.0 (C_4), 148.7 (C_6),152.7 (C_2), 169.4 (C=O), 194.8 (C=O). HRMS *m*/*z* 268.1212; calcd for $C_{16}H_{16}N_2O_2$ 268.12063.

***N*,*N*-Diethyl-2-phenyl-3-oxo-3-(2-pyridyl)propionamide (8d).** Yield 19% (reaction for 3 d); δ_H (400 MHz, $CDCl_3$) 1.04 (t, 3H, *J* 7, CH_3), 1.23 (t, 3H, *J* 7, CH_3), 3.30–3.35 (m, 4H, CH_2), 6.24 (s, 1H, CH), 7.33–7.39 (m, 5H, phenyl-H), 7.44 (t, 1H, C_5-H), 7.81 (td, 1H, C_4-H), 8.07 (dd, 1H, C_3-H), 8.62 (dd, 1H, C_6-H); δ_C (400 MHz, $CDCl_3$) 12.6 (CH_3), 13.6 (CH_3), 40.2 (CH_2), 42.8 (CH_2), 57.3 (CH), 122.5 (C_3), 126.9 (C_5), 127.6, 128.6, 129.78, 134.1, 137.0 (C_4), 148.4 (C_6),153.1 (C_2), 168.4 (C=O), 194.9 (C=O). HRMS *m*/*z* 296.1523; calcd for $C_{18}H_{20}N_2O_2$ 296.15193.

2-Methyl-1-morpholino-3-(2-pyridyl)propane-1,3-dione (11b). Yield = 100% (reaction for 17 h); δ_H (200 MHz, $CDCl_3$) 1.351 (d, 3H, *J* 7, CH_3), 3.46–3.76 (m, 8H), 4.89 (q, 1H, *J* 7, CH), 7.40 (t, 1H, C_5-H), 7.79 (td, 1H, C_4-H), 7.97 (dd, 1H, C_3-H), 8.55 (dd, 1H,C_6-H); δ_C (200 MHz, $CDCl_3$) 12.8 (CH_3), 42.0, 43.8 (CH), 46.6, 66.3, 66.5, 122.1 (C_3), 127.1 (C_5), 136.9 (C_4), 148.5 (C_6), 151.9 (C_2), 170.6 (C=O), 197.0 (C=O). HRMS *m*/*z* 248.1150; calcd for $C_{13}H_{16}N_2O_3$ 248.11554.

1-Morpholino-2-phenyl-3-(2-pyridyl)propane-1,3-dione (11d). Yield 59% (reaction for 23 h); δ_H (200 MHz, $CDCl_3$) 3.25–3.69 (m, 8H), 6.22 (s, 1H, CH), 7.19–7.43 (m, 6H, C_5-H, phenyl-H), 7.76 (td, 1H, C_4-H) , 8.00 (dd, 1H, C_3-H), 8.57 (dd, 1H, C_6-H); δ_C (200 MHz, $CDCl_3$) 42.3, 46.7, 56.2 (CH), 66.1, 66.5, 122.4 (C_3), 127.2 (C_5), 127.7, 128.4, 129.6, 133.2, 137.0 (C_4), 148.6 (C_6), 152.4 (C_2), 168.0 (C=O), 194.4 (C=O). HRMS *m*/*z* 310.1308; calcd for $C_{18}H_{18}N_2O_3$ 310.13119.

2-Phenyl-3-(2-pyridyl)-1-pyrrolidinopropane-1,3-dione (10d). Yield 85% (reaction for 5 min); δ_H (200 MHz, $CDCl_3$) 1.74–1.95 (m, 4H), 3.25–3.52 (m, 4H), 6.10 (s, 1H, CH), 7.21–7.41 (m, 6H, C_5-H, phenyl-H), 7.73 (td, 1H, C_4-H), 8.03 (dd, 1H, C_3-H), 8.59 (dd, 1H, C_6-H); δ_C (200 MHz, $CDCl_3$) 24.3, 25.9, 45.9, 46.9, 58.5 (CH), 122.5 (C_3), 127.1 (C_5), 127.5, 128.4, 130.0, 133.3, 137.0 (C_4), 148.7 (C_6), 152.7 (C_2), 167.5 (C=O), 194.7 (C=O). HRMS *m*/*z* 294.1358; calcd for $C_{18}H_{18}N_2O_2$ 294.136279.

General procedure for the hydrolysis of mesoionic compounds 5 to 2-acylpyridines 12

To 6 mg of 2,3-dihydro-3-oxo-2-R-1*H*-4λ^5-pyrrolo[1,2-*a*]-pyridin-4-ylium-1-olate were added 10 drops of 1% aqueous NaOH solution. The mixture was stirred overnight at room temperature under N_2, neutralised, and extracted with ether. The organic layer was dried over $MgSO_4$, filtrated and evaporated. If necessary, the crude product was purified by column chromatography (silica gel 60 mesh; $AcOCH_3$). Structures and purities were confirmed by GC-MS, ^1H and ^{13}C NMR, and comparison with literature data.[16] Yields (not optimised): **12a** 99%, **12b** 63%, **12c** 84%, **12d** 95%.

Matrix IR spectra and calculated IR spectra of 5a and 4a (13a)

Mesoion **5a** was isolated in an Ar matrix by subliming it at 100 °C in a stream of Ar. The resulting IR spectrum is shown in Fig. 1b: 1794/1783, 1676, 1610, 1585, 1480, 1450, 1340, 1243, 1183, 1103, 1054, 779, 738, 687, 559, 491 cm^{-1}. The weak signal at 2142 cm^{-1} is ascribed to ketene **4a**. The same spectrum, with a slightly stronger ketene signal, is obtained by FVT of **3a** at 650 °C with matrix isolation of the product at 15 K. Calculated[7] IR frequencies for **5a** at the B3LYP/6-31G* level are scaled by a factor 0.9613, and bands with intensities below 7 km mol^{-1} are ignored. The spectra were calculated for a relative permittivity $\varepsilon = 1$ (gas phase) and for $\varepsilon = 40$, simulating a highly polar environment.[9] The higher frequency C=O stretching vibration at 1814/1794 cm^{-1} (for $\varepsilon = 1$ and 40, respectively) corresponds to the ylidic "lactam" carbonyl, C3. The lower frequency carbonyl vibration at 1693/1681 cm^{-1} corresponds to the C1 ketone. Calculated IR spectrum of **5a** (wavenumber/cm^{-1} for $\varepsilon = 1$, wavenumber for $\varepsilon = 40$, (intensity/km mol^{-1} for $\varepsilon = 1$, intensity for $\varepsilon = 40$) given): 1814, 1794 (394, 497); 1693, 1681 (517, 914); 1597, 1595 (99, 208); 1576, 1571 (38, 72); 1458, 1460 (13, 20); 1337, 1339 (25, 51); 1214, 1219 (98, 221); 1154, 1156 (25, 31); 1085, 1087 (17, 37); 1019, 1025 (54, 113); 1004, 1006 (12, 18); 768, 776 (22, 27); 746, 750 (11, 7); 712, 702 (81, 104); 659, 672 (27, 51); 539, 544 (27, 34); 463, 472 (42, 60).

Broad band irradiation with the Hg/Xe lamp caused an increase in the intensity of the ketene band at 2142 cm^{-1} with concomitant decrease in the bands due to **5a**. A drastic increase in the ketene band resulted after 25 min of irradiation, and only little further increase resulted after a further 35 min. IR spectrum of the resulting ketene (Fig. 2b): 2143s, 2122w–m, 1663w–m, 1592w, 1585w, 1443w, 1380m, 1224w, 1069w, 1002w, 992w, 875w, 746w, 702 w, 694w, 560 w. The bands at 3730 and 1610 cm^{-1} are due to water. Calculated[7] IR frequencies at the B3LYP/6-31G* level are scaled by a factor 0.9613, and bands with intensities below 6 km mol^{-1} are ignored. Calculated IR spectrum of **13a** (gas phase; wavenumber/cm^{-1} (intensity/km mol^{-1}) given): 3109 (47), 3092 (19), 3075 (11), 2147 (1169), 1669 (167), 1577 (17), 1566 (20), 1423 (28), 1370 (464), 1201 (34),

1079 (34), 984 (33), 973 (42), 857 (25), 738 (35), 695 (60), 692 (23), 609 (8), 597 (11), 549 (11), 211 (11).

Acknowledgements

We thank the Australian Research Council, the National University of Singapore, and The University of Queensland for Financial Support.

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Paper a906831g