Azafulvenium methides: new extended dipolar systems

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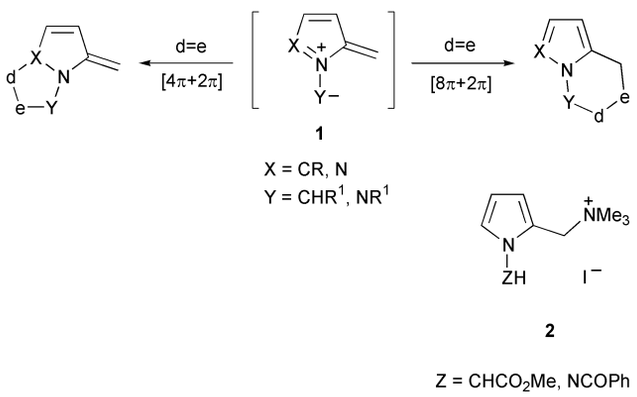
The transient 1-azafulvenium methides **24**, **26** and **28** generated by thermal extrusion of sulfur dioxide from pyrrolo[1,2-*c*][1,3]thiazole 2,2-dioxide **20** (R = Me), **22** and **23** undergo sigmatropic [1,8]H shifts and the 1-acyl derivatives **30** electrocyclise to give novel pyrrolo[1,2-*c*][1,3]oxazines **32**. The analogous 1,2-diazafulvenium methide **36** has been intercepted in [8π + 2π] cycloadditions with electron-rich silylated acetylenes to give adducts **37**–**40**. This behaviour is partially explained by Frontier MO theory.

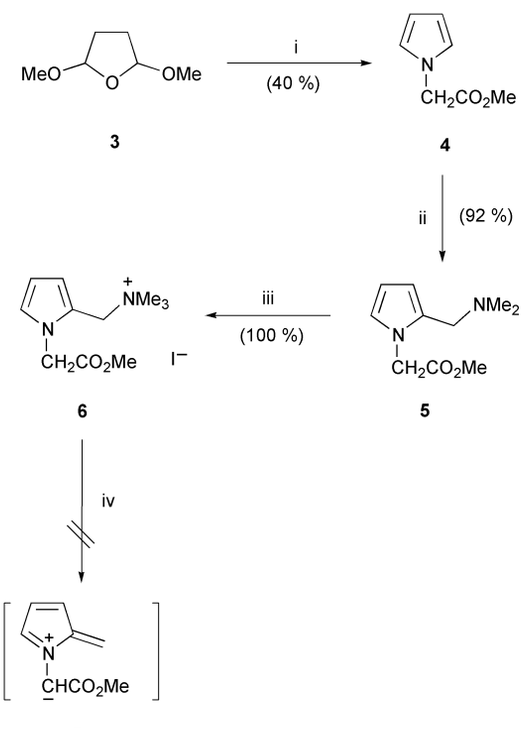
Introduction

In a preliminary communication,[1] we presented the first evidence for trapping of the transient 1-aza- and 1,2-diazafulvenium methide systems **1** in a number of pericyclic reactions. Here we report full details of our study of these interesting systems which, in principle, can act as 4π 1,3-dipoles or as 8π 1,7-dipoles.



Results and discussion

Dipolar systems **1** (X = CH, Y = CHR[1]) can be considered as "higher-order" azomethine ylides and initially we hoped to extend the standard base catalysed elimination route to simple azomethine ylides to generate **1** from the corresponding quaternary ammonium salt **2**. In a preliminary investigation quaternary salts **2** (Z = CH_2, CHPh) were isolated as unstable solids, by quaternisation of the respective Mannich bases (obtained from the corresponding *N*-substituted pyrroles). All attempts to produce the desired systems **1** (X = CH, Y = CH_2, CHPh) by treatment of **2** (Z = CH_2, CHPh) with DBU, LDA or potassium *tert*-butoxide, were unsuccessful. A possible explanation for the inability to generate **1** (X = CH, Y = CH_2, CHPh) lies in the low "acidity" of the methylene protons attached at position-1. An *N*-substituted pyrrole precursor which incorporated an electron-withdrawing function on the exocyclic carbon (Z = $CHCO_2Me$) was therefore studied.



Scheme 1 *Reagents and conditions*: i, $NH_2CH_2CO_2Me$·HCl–AcOH–KOAc, reflux; ii, CH_2O (aq.)–$NHMe_2$·HCl; iii, MeI–EtOH; iv, base–solvent (see text).

(*N*-Methoxycarbonylmethylpyrrol-2-ylmethyl)trimethylammonium iodide **6** was obtained from 2,5-dimethoxytetrahydrofuran **3** as shown (Scheme 1) and its structure readily established by ^{1}H NMR spectroscopy. The quaternary salt **6** was suspended in anhydrous solvent (THF, MeCN or DMSO) with the desired dipolarophile (2 eq.) and the appropriate base (DBU ‡, LDA, KO^{t}Bu) (1 eq.) added. The reactions were monitored by TLC [SiO_2, ethyl acetate–hexane (1 : 1)] over four hours. Following work-up, the crude reaction mixture was examined by ^{1}H NMR spectroscopy; however, although **6** was consumed during the course of four hours (both at standard

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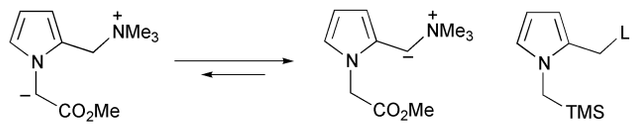
‡ CAUTION! DBU reacts vigorously and exothermically with *N*-phenylmaleimide and so was not used in combination with this dipolarophile.

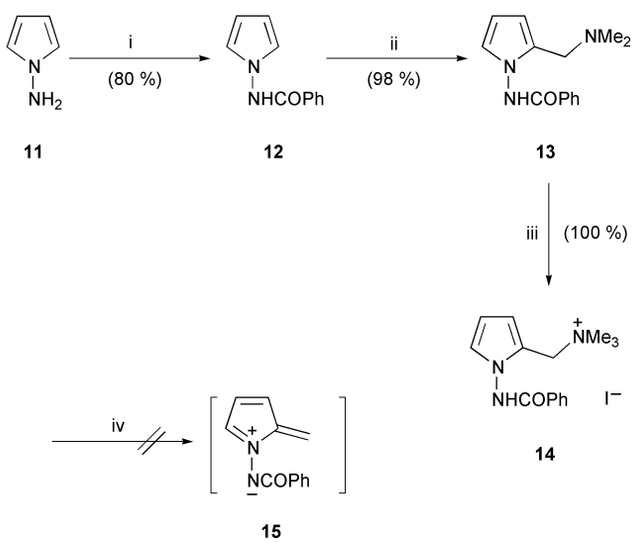
and elevated temperatures), there was no evidence that the dipolar system **7** (if generated) participates in an intermolecular cycloaddition with *N*-phenylmaleimide, diethyl fumarate or DMAD under these conditions.



8 **9** **10**

A possible reason for our inability to form 1-azafulvenium methide **7** lies in the "acidic" nature of the protons attached to the methylene group at C-2. Proton removal from the salt **6** could lead to the desired anion **8** and hence **7** but, due to the relative pK_a's of the protons at positions-1 and -2, may well lead to the ylide **9** from which elimination is precluded. Padwa *et al.*[2] suggested a similar explanation for their failure to generate **1** (X = CH, Y = CH_2) in the fluoride ion induced desilylation of pyrroles **10** (L = OMe, CN, SPh, SO_2Ph).

Increasing the acidity of the protons at position-1 should favour the desired elimination and to this end the quaternary ammonium salt **14** was prepared from *N*-aminopyrrole **11** (Scheme 2). In this case the tendency for deprotonation at



11 **12** **13** **14** **15**

Scheme 2 *Reagents and conditions*: i, KOH (aq.)–PhCOCl; ii, Eschenmoser's salt–MeCN; iii, MeI–EtOH; iv, base–solvent (see text).

position-1 rather than at position-2 would be enhanced due to the greater difference in relative pK_a's of these positions *i.e.* NH is more "acidic" than CH_2.

The quaternary salt **14** was suspended in anhydrous solvent (THF, MeCN) with the desired dipolarophile (2 eq.) (*N*-phenylmaleimide, diethyl fumarate and DMAD) and the appropriate base (1 eq.) (DBU, LDA, $(^iPr)_2NEt$) added. However, again there was no evidence for interception of the dipolar system **15** with any of the dipolarophiles at either standard or elevated temperatures. In view of this consistent failure to produce the desired dipolar system by base catalysed elimination we turned to an alternative approach.

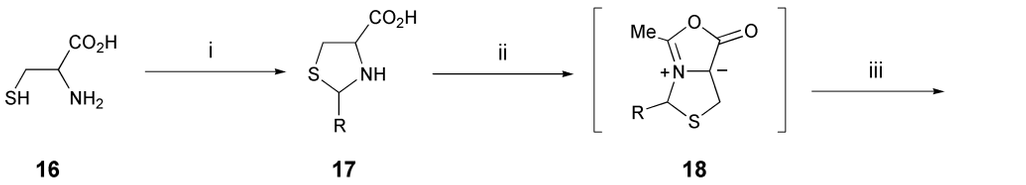
The cheletropic extrusion of sulfur dioxide from heterocyclic sulfones is now one of the most widely used and flexible routes for the generation of short-lived reactive dienes such as the heterocyclic *o*-quinodimethanes. This method has been well documented[3] and is attractive since, in general, heterocyclic sulfones are stable, crystalline materials which can be easily handled and readily prepared.

1-Azafulvenium methides such as **1** or **7** can be thought of as special heterocyclic analogues of *o*-quinodimethane. The first attempt to produce such a species by extrusion of sulfur dioxide from a sulfone was reported by Padwa *et al.*[2] However, their attempts to generate **21** (R = H) by extrusion of sulfur dioxide from sulfone **20** (R = H) were unsuccessful due to the high thermal stability of the sulfone. This stability is not surprising in view of the low bond order of the 3,4 bond of the sulfolene moiety and temperatures higher than those conveniently accessible in a solution phase thermolysis are likely to be required. Our experience with the extrusion of sulfur dioxide from heterocyclic sulfones and with flash vacuum pyrolysis (FVP) therefore led us to reinvestigate this approach.

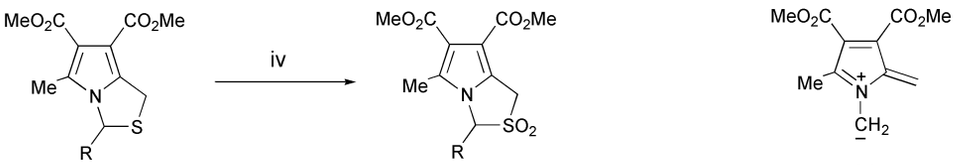
The sulfone **20** (R = H) was prepared from L-cysteine using the method of Padwa[2] as shown in Scheme 3. The thiazolidine carboxylic acid **17** (R = H), obtained by reaction of the cysteine with formaldehyde, was heated in the presence of acetic anhydride and dimethyl acetylenedicarboxylate to give the sulfide **19** by dipolar cycloaddition of the acetylene to the intermediate dipole **18**. The sulfide was finally converted to the sulfone by oxidation with 3-chloroperbenzoic acid. Again, in our hands this sulfone did not extrude sulfur dioxide when heated in solution at 300 °C. However, on FVP at 700 °C/10^{-3} mmHg sulfur dioxide was eliminated although no identifiable products arising from the dipole were detected on the cold receiver. Attempts were made to trap the azafulvenium methide **21** by cycloaddition on the cold receiver by co-condensation of the pyrolysate at −180 °C with methyl vinyl ketone or by condensation in a matrix with dichloromethane which was allowed to thaw and mix with a solution of *N*-phenylmaleimide or DMAD below −100 °C. No evidence was obtained for the formation of adducts.

Encouraged by the extrusion of sulfur dioxide we designed derivatives for which the formation of the dipole might be revealed by intramolecular trapping in the FVP experiment. Sulfones **20** (R = Me, Ph, 4-$MeOC_6H_4$, 2-thienyl) bearing substituents at the 3-position of the 1*H*,3*H*-pyrrolo[1,2-*c*]-[1,3]thiazole ring were easily prepared from the corresponding 2-substituted thiazolidine-4-carboxylic acids **17** (obtained by condensing L-cysteine **16** with the appropriate aldehyde), in most cases in relatively high yield (Scheme 3). Sulfones bearing simple alkyl groups at the 1-position of the 1*H*,3*H*-pyrrolo-[1,2-*c*][1,3]thiazole ring were easily obtained by metallation of sulfone **20** (R = H) with LiHMDS and subsequent quenching with iodomethane (Scheme 4). Substitution occurs selectively at C-1 rather than at C-3 due to the additional stabilising effect of the ester functionality at C-7 on the α-sulfonyl carbanion.

None of the 3-aryl derivatives on FVP gave products resulting from electrocyclisation involving the aryl ring of the type seen with aryl *o*-quinodimethanes.[4] On the other hand, both the 1- and 3-methyl sulfones gave more promising results. Thus FVP (700 °C/10^{-3} mmHg) of sulfones **20** (R = Me) and **22** gave the vinylpyrroles **25** and **27** respectively, formation of which can be explained by allowed suprafacial [1,8]H shifts in the 8π 1,7-dipolar systems **24** and **26** (Scheme 5). The reaction of the 3-methyl derivative **20** (R = Me) to give the *N*-vinylpyrrole **25** was clean but in the case of the 1-methyl compound **22** the 2-vinylpyrrole **27**, was not obtained pure. However, the ^1H NMR spectrum of the contaminated impure product was clearly consistent with the vinylpyrrole structure which was also supported by the mass spectrum. Concerted sigmatropic shifts can only occur when the methyl groups adopt an inward, *Z*-configuration. In a delocalised dipolar system there will be a barrier to rotation around the partial double bonds but rotation at the high temperatures of the FVP experiment is not unreasonable. The difference between the two derivatives **20** (R = Me) and **22** may reflect the differing ease with which the dipoles can attain the required configurations having inward methyl groups (only the *Z*-configurations are illustrated in Scheme 5). In view of this configurational problem we prepared a sample of the 1,1-dimethylsulfone **23** (obtained by metallation of **22** and subsequent reaction with iodomethane) (Scheme 4). Significantly, on FVP, the 1,1-dimethyl derivative



16 17 18

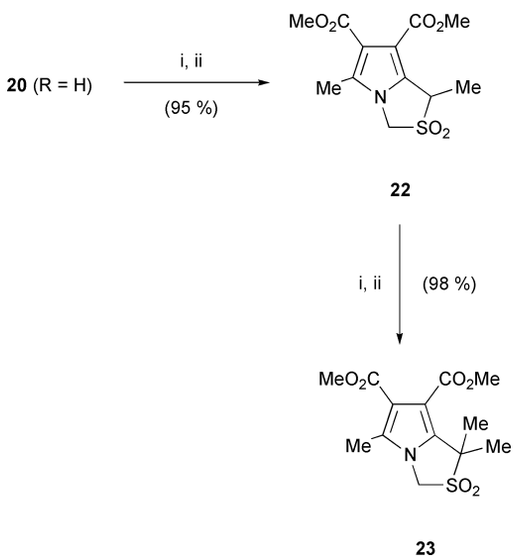


19 20

% Yield

R	17	19	20
H	74	55	99
Me	62	40	95
Ph	67	68	94
p-Anisyl	75	57	95
2-Thienyl	94	40	98

Scheme 3 *Reagents and conditions*: i, RCHO; ii, Ac_2O, reflux; iii, DMAD; iv, MCPBA–CH_2Cl_2.



Scheme 4 *Reagents and conditions*: i, LiHMDS–THF, −78 °C, 1 h; ii, MeI, −78 °C–rt.

23 (where one of the methyl groups in **28** must necessarily be inward) occurred cleanly to give the 2-isopropenylpyrrole **29**, without any of the complications associated with the pyrolysis of **22**.

Although our attempts to intercept the desired 1-azafulvenium methide *via* an electrocyclisation reaction with simple aryl groups had been disappointing, there is precedent for the electrocyclisation of dipolar systems involving carbonyl groups.[5] To this end the 1-benzoyl derivative **30** (R = Ph) (Scheme 6) was prepared by treatment of the sulfone **20** (R = H) with LiHMDS (1 eq.) followed by freshly distilled benzoyl chloride (1.0 eq.). However, it was observed that repetition of this reaction under identical conditions gave inconsistent yields of the desired product **30** (R = Ph). We attribute this to a competing proton transfer between the α-sulfonyl carbanion and the acylated product **30** (R = Ph). In order to facilitate a clean and optimised transformation, we examined the use of other bases (LDA) and electrophiles (methyl benzoate and *N*-methoxy-*N*-methylbenzamide)§ under a variety of conditions. The optimum conditions were found to be sequential treatment of **20** with a base (1.0 eq.) and acyl chloride (1.0 eq.) followed by further equivalents of base and acyl chloride. By using this methodology we prepared a range of 1-acyl derivatives **30** (Scheme 6).

On FVP (600 °C/10^{-3} mmHg) the benzoyl derivative **30** (R = Ph) gave the 1*H*-pyrrolo[1,2-*c*][1,3]oxazine **32** (R = Ph), the first example of this new ring system and further strong evidence for the generation of the desired 1-azafulvenium methide dipolar system **31**. Significantly, introduction of the acyl group lowers the temperature required for the extrusion of sulfur dioxide and the reaction can be carried out in solution at 200 °C (Scheme 6). With exception of the 1-methoxycarbonyl derivative **30** (R = OMe) the reaction is general for all the acyl derivatives.

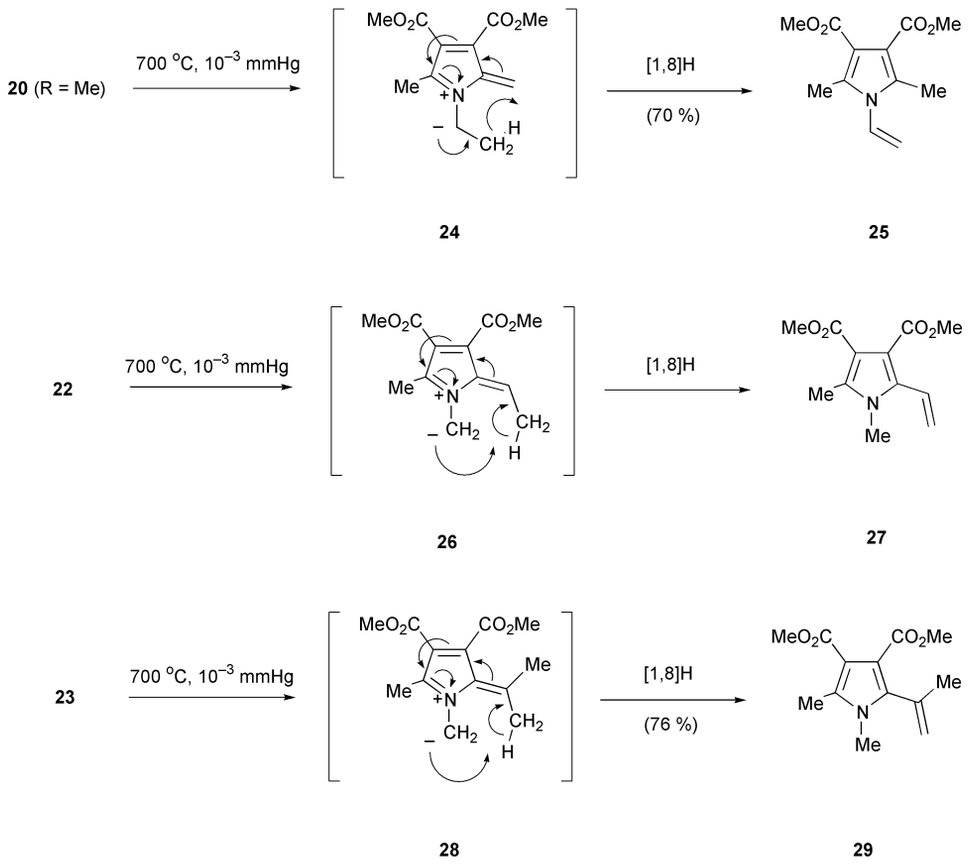
Since the dipole can be generated in solution, intermolecular trapping in a cycloaddition becomes a possibility. However, extrusion of sulfur dioxide from **30** (R = Ph) at 200 °C in trichlorobenzene in the presence of *N*-phenylmaleimide, DMAD or bis(trimethylsilyl)acetylene gave only the 1*H*-pyrrolo[1,2-*c*][1,3]oxazine **32** (R = Ph) and no trace of cycloadduct. Prolonged heating of the 1*H*-pyrrolo[1,2-*c*][1,3]oxazine **32** (R = Ph) in the presence of the dipolarophiles resulted in recovery of starting material and there was no evidence for reversibility in the electrocyclic ring closure.

We consider the formation of the 1*H*-pyrrolo[1,2-*c*]-[1,3]oxazines to be strong evidence for the generation of 1-azafulvenium methide. Mechanistically both the sigmatropic hydrogen transfer and the electrocyclisation reactions can be rationalised by a concerted loss of sulfur dioxide and concomitant rearrangement of the dipolar intermediate.

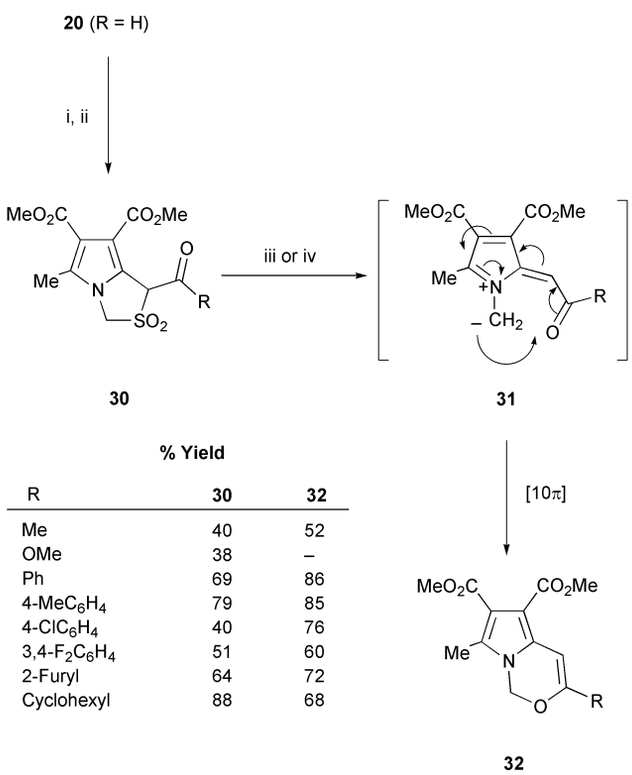
The analogous pyrazole sulfone **35** is a potential precursor to the diazafulvenium methide **36**. It was obtained by oxidation of the pyrazolo[1,5-*c*][1,3]thiazole **34**, which we have described elsewhere,[6] with MCPBA (Scheme 7). Significantly, extrusion of sulfur dioxide from this sulfone occurs more easily than from sulfone **30** (R = H) and can be achieved in solution; the extra pyrazole ring nitrogen thus appears to exert the same effect as an electron withdrawing acyl group attached to the pyrrole system.

Heating of sulfone **35** in refluxing 1,2,4-trichlorobenzene (or toluene in a sealed tube at 300 °C) in the presence of *N*-phenylmaleimide or dimethyl acetylenedicarboxylate gave no adducts. However, bis(trimethylsilyl)acetylene, which has been shown to be a reactive electron-rich dipolarophile at high

§ The α-sulfonyl carbanion reacts slowly with methyl benzoate and not at all with *N*-methoxy-*N*-methylbenzamide and electrophilic substitution can only be achieved by employing the more reactive acyl chlorides.

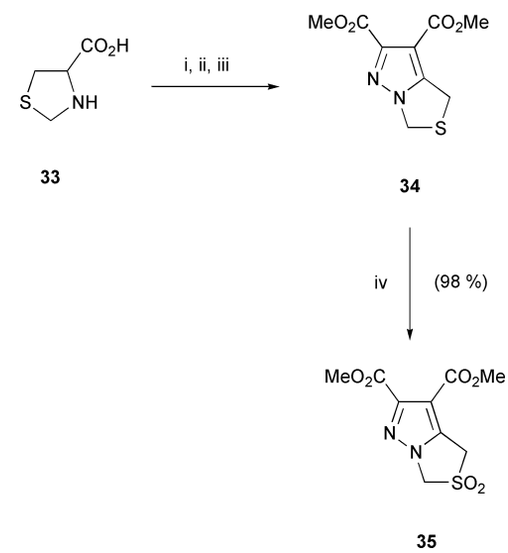


Scheme 5



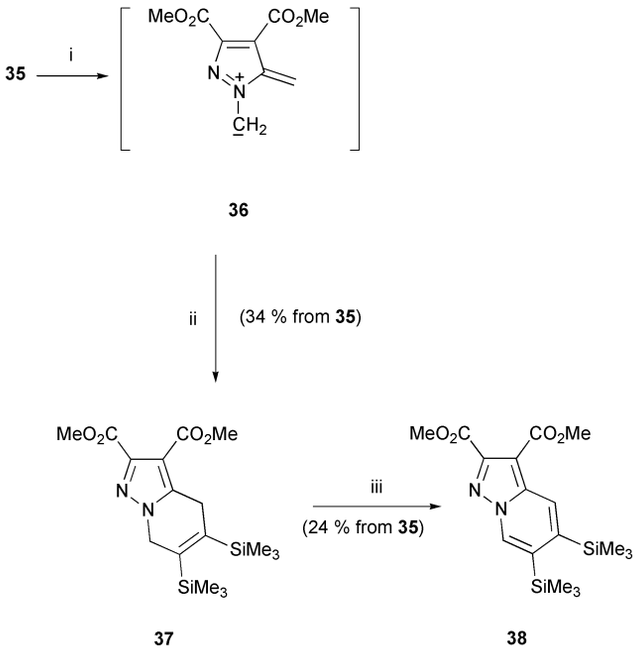
% Yield		
R	30	32
Me	40	52
OMe	38	–
Ph	69	86
4-MeC_6H_4	79	85
4-ClC_6H_4	40	76
3,4-$F_2C_6H_4$	51	60
2-Furyl	64	72
Cyclohexyl	88	68

Scheme 6 *Reagents and conditions*: i, LiHMDS–THF; ii, RCOCl; iii, 600 °C/10^{-3} mmHg [**32** (R = Ph) only]; iv, 200 °C, 1,2,4-trichlorobenzene.

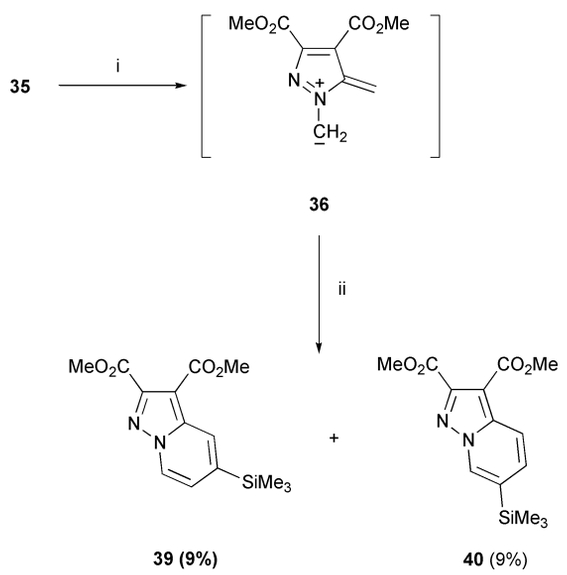


Scheme 7 *Reagents and conditions*: i, $NaNO_2$–HCl; ii, TFAA–Et_2O; iii, DMAD–xylene–reflux; iv, MCPBA–CH_2Cl_2.

temperatures in Diels–Alder reactions with inverse electron demand,[7] gave the cycloadduct **37** in 34% yield after three hours. This provides the first evidence for the formation of these dipolar systems by intermolecular trapping (Scheme 8). Prolonged heating, under identical conditions afforded the aromatised adduct **38** in 24% yield (Scheme 8). Pyrolysis of the sulfone **35** (in a sealed tube of toluene, 300 °C) in the presence of the unsymmetrical dipolarophile (trimethylsilyl)acetylene gave a mixture of the aromatised regioisomers **39** and **40** (Scheme 9) which could be separated by chromatography [SiO_2, ethyl acetate–petroleum ether (1 : 1)]. Tentative assignment of **39** and **40** as the 5- and 6-substituted pyrazolo[1,5-*a*]pyridines respectively was made on the basis that the H-7 usually occurs at the lowest field in this system and, typically, the coupling constant $J_{4–5}$ is 9 Hz and $J_{6–7}$ is 7 Hz.[8] Signals for aromatic CH appeared in the spectrum of isomer **39** at δ 8.50 (d, $J = 7$ Hz), 8.30 (s) and 7.11 (d, $J = 7$ Hz) and in that of isomer **40** at δ 8.50 (s), 8.14 (d, $J = 9$ Hz), and 7.47 (d, $J = 9$ Hz) consistent with this pattern. Other electron-rich dipolarophiles such as



Scheme 8 *Reagents and conditions*: i, 230–300 °C; ii, 3 h in the presence of bis(trimethylsilyl)acetylene at 230–300 °C; iii, heating for a further 3 h at 230–300 °C.



Scheme 9 *Reagents and conditions*: i, 300 °C; ii, trimethylsilylacetylene.

1-pyrrolidinocyclopentene and 1-pyrrolidinocyclohexene and tributylstannylacetylene failed to give isolable adducts.

It may be significant that the dipolar system **36** undergoes cycloaddition only with electron-rich dipolarophiles and that the addition occurs across the 1,7- and not the 1,3-positions. The semi-empirical molecular orbital package MOPAC/PM3[9] was used to calculate the atomic orbital coefficients in the HOMO and LUMO of the 1-aza- and 1,2-diazafulvenium methides **21** and **36** (Fig. 1).

Employing the same package the HOMO and LUMO energies for DMAD (HO = −11.7 eV, LU = −1.0 eV), bis-(trimethylsilyl)acetylene (HO = −9.5 eV, LU = 1.2 eV) and (trimethylsilyl)acetylene (HO = −10.1 eV, LU = 1.2 eV) were calculated. These data suggest that additions of DMAD to both **21** and **36** would be dipole-HOMO controlled, whilst addition to the electron-rich dipolarophiles would be dipole-LUMO controlled. By comparing the two extended dipoles **21** and **36**, it can be seen that the larger coefficients reside on C-1 and C-3 in the HOMO and on C-1 and C-7 in the LUMO in each case. One would therefore expect additions to electron-

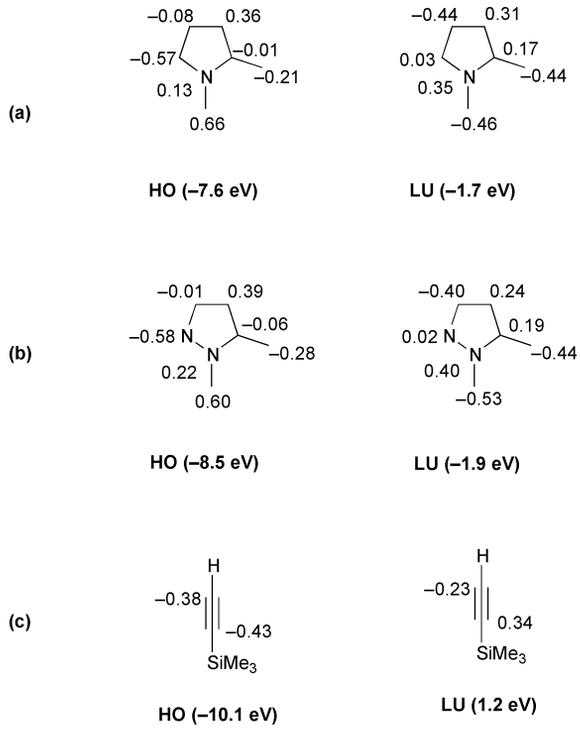


Fig. 1 MO coefficients of dipoles **21** (a), **36** (b) and trimethylsilylacetylene (c).

deficient dipolarophiles such as DMAD to occur *via* the [4π + 2π] mode (*i.e.* the dipoles would act as simple 1,3-dipoles) whilst electron-rich dipolarophiles would be expected to undergo additions *via* the [8π + 2π] mode (*i.e.* the dipoles would act as extended 1,7-systems). This model is consistent with the site selectivity observed in the additions of **36** to electron-rich dipolarophiles.

The question of why the addition of (trimethylsilyl)acetylene to **36** is apparently non-regiospecific can also be explained by the relative sizes of the coefficients in the dominant orbital interaction between these reactants. The HOMO and LUMO coefficients of (trimethylsilyl)acetylene are as shown. The coefficients at C-1 and C-7 in the LUMO of **36** are −0.53 and −0.44, and −0.38 and −0.43 for the HOMO of trimethylsilylacetylene, and these small differences in the size of the coefficients on both the dipole and the dipolarophile can therefore account for the lack of regioselectivity observed in the dipole LUMO controlled additions of **36** to this acetylene.

These MO calculations go some way towards rationalising the behaviour of dipoles **21** and **36**. Thus, the observation of 1,7-addition of bis(trimethylsilyl)acetylene to **36** but not to **21** is consistent with the lower LUMO of the former making the LUMO controlled reactions with this electron-rich dipolarophile more favourable. It also accounts for the lack of regioselectivity in the dipole-LUMO controlled additions of **36**. However, the prediction is that dipole-HOMO controlled addition to DMAD and other electron-deficient dipolarophiles should also be favourable, especially for **21**. The fact that no adducts are observed is therefore puzzling. It may be that since the prediction is for dipole-HOMO controlled additions to occur across the 1,3-positions that adducts of this type do form but lack sufficient stability for isolation.

Experimental

^{1}H NMR spectra were recorded on either a Bruker ACE 200 (200 MHz) instrument or a Varian Gemini 300 (300 MHz) instrument. ^{13}C and ^{13}C DEPT spectra were recorded on the Varian Gemini 300 (300 MHz) instrument. All spectra were recorded using tetramethylsilane (TMS) as the internal reference. Infra-red spectra were recorded in the range of 4000 to

600 cm^{-1} using a Perkin-Elmer 298 instrument. Mass spectra were recorded on a VG Analytical 7070E or a Trio 1000 Quadrapole GC mass spectrometer. Microanalyses were performed in the University of Liverpool Department of Chemistry microanalytical laboratory using a Carlo Erba elemental analyzer and melting points were determined using a Gallenkamp melting point apparatus and are uncorrected. All reagents were of commercial quality and solvents were dried, where necessary, using standard procedures.

N-(Methoxycarbonylmethyl)pyrrole (4)[10]

Glycine methyl ester hydrochloride (6.28 g, 50 mmol) and potassium acetate (8.02 g, 82.0 mmol) were dissolved in the minimum amount of distilled water and added to glacial AcOH (50 mL). The mixture was then heated to reflux and 2,5-dimethoxytetrahydrofuran (6.5 mL, 50 mmol) added. After heating for 4 h, the reaction mixture was cooled, neutralised with solid $NaHCO_3$ and extracted with EtOAc (3 × 100 mL). The combined organic fractions were then thoroughly washed with water (100 mL) and brine (100 mL) and dried over anhydrous $MgSO_4$. Removal of the solvent *in vacuo* gave a dark oil which was purified by column chromatography [SiO_2, diethyl ether–hexane (1 : 1)] to give *N-(methoxycarbonylmethyl)pyrrole* (2.78 g, 40%) as a pale yellow oil (Found: C, 60.3; H, 6.4; N, 10.1. $C_7H_9NO_2$ requires C, 60.4; H, 6.5; N, 10.1%); ν_{max} (neat) 1754 (C=O) cm^{-1}; δ_H ($CDCl_3$)[10b] 3.74 (s, 3H, $CH_2CO_2CH_3$), 4.62 (s, 2H, $CH_2CO_2CH_3$), 6.20 and 6.65 (AA′, XX′, 4H, Ar-H); δ_C ($CDCl_3$) 50.8 (CH_2), 52.5 (CH_3), 109.3 (CH), 122.0 (CH) and 169.5 (C=O).

2-Dimethylaminomethyl-*N*-(methoxycarbonylmethyl)pyrrole (5)

Dimethylamine hydrochloride (0.79 g, 9.7 mmol) was dissolved in formaldehyde (0.73 mL, 40% aq. soln., 9.7 mmol) and cooled to 0 °C. *N*-(Methoxycarbonylmethyl)pyrrole (1.35 g, 9.7 mmol) was slowly added and the mixture stirred vigorously for 3 h, not allowing the temperature to exceed 60 °C. The now homogeneous mixture was left to stand for 12 h, poured onto pre-cooled 30% (w/v) NaOH solution and extracted with dichloromethane (3 × 100 mL). The combined organic fractions were then thoroughly washed with water (100 mL) and brine (100 mL) and dried over anhydrous $MgSO_4$. Removal of the solvent *in vacuo* gave *2-dimethylaminomethyl-N-(methoxycarbonylmethyl)pyrrole* (1.62 g, 92%) as a pale yellow oil (Found: C, 61.1; H, 8.1; N, 14.3. $C_{10}H_{16}N_2O_2$ requires C, 61.2; H, 8.2; N, 14.3%); ν_{max} (neat) 1757 (C=O) cm^{-1}; δ_H ($CDCl_3$) 2.12 (s, 6H, $N(CH_3)_2$), 3.30 (s, 2H, $CH_2N(CH_3)_2$), 3.72 (s, 3H, $CH_2CO_2CH_3$), 4.75 (s, 2H, $CH_2CO_2CH_3$), 6.01 (d, 1H, 3-H), 6.09 (t, 1H, 4-H) and 6.62 (d, 1H, 5-H); δ_C ($CDCl_3$) 44.9 (CH_2), 48.7 (CH_2), 52.2 (CH_3), 55.9 (CH_3), 107.5 (CH), 109.7 (CH), 123.0 (CH), 130.3 and 170.1 (C=O).

(*N*-Methoxycarbonylmethylpyrrol-2-ylmethyl)trimethylammonium iodide (6)

2-Dimethylaminomethyl-*N*-(methoxycarbonylmethyl)pyrrole (1.02 g, 5.2 mmol) was dissolved in absolute ethanol (10 mL) and cooled to 0 °C. A solution of iodomethane (0.92 g, 6.5 mmol) in absolute ethanol (5 mL) was added slowly dropwise. After the addition was complete, the mixture was stirred vigorously for 2 h and allowed to warm to room temperature for 2 h and then placed in the freezer overnight. Diethyl ether (25 mL) was then added and the solid product filtered off and recrystallised from diethyl ether to give *(N-methoxycarbonylmethylpyrrol-2-ylmethyl)trimethylammonium iodide* (1.76 g, 100%) as a pale yellow solid, mp dec. 145–148 °C (Found: C, 39.3; H, 5.8; N, 8.1. $C_{11}H_{19}IN_2O_2$ requires C, 39.1; H, 5.7; N, 8.3%); ν_{max} (Nujol) 1749 (C=O) cm^{-1}; δ_H (D_2O) 3.07 (s, 9H, $N^+(CH_3)_3$), 3.79 (s, 3H, $CH_2CO_2CH_3$), 4.51 (s, 2H, $CH_2N^+(CH_3)_3$), 5.04 (s, 2H, $CH_3CO_2CH_3$), 6.39 (d, 1H, 3-H), 6.62 (t, 1H, 4-H) and 7.03 (d, 1H, 5-H); δ_C (D_2O) 47.5 (CH_2), 51.2 (CH_2), 52.7 (CH_2), 59.5 (CH_2), 108.8 (CH), 116.3 (CH), 126.8 (CH), 134.3 and 174.1 (C=O); *m/z* 211 (M^+, 40%), 152 (100).

2-Dimethylaminomethyl-*N*-benzamidopyrrole (13)

A solution of dimethyl(methylene)ammonium iodide (Eschenmoser's salt) (1.98 g, 11 mmol) dissolved in the minimum of anhydrous acetonitrile was slowly added to a solution of *N*-benzamidopyrrole[11] (2.0 g, 11 mmol) dissolved in anhydrous acetonitrile (25 mL) over a period of thirty minutes. The reaction mixture was then stirred at room temperature for twenty four hours, and then basified with 30% (w/v) sodium hydroxide solution. The organics were extracted with ethyl acetate (3 × 100 mL), washed with water (100 mL), brine (100 mL) and dried over anhydrous $MgSO_4$. The solvents were removed *in vacuo* to give *2-dimethylaminomethyl-N-benzamidopyrrole* (2.56 g, 98%) as an off-white moisture sensitive solid (Found: C, 69.3; H, 7.3; N, 17.2. $C_{14}H_{17}N_3O$ requires C, 69.1; H, 7.0; N, 17.3%); δ_H ($CDCl_3$) 2.22 (s, 6H, $N(CH_3)_2$), 3.34 (s, 2H, CH_2), 6.07–6.14 and 6.90–6.92 (m, 3H, pyrrole-H), 7.45–7.59 and 7.93–7.94 (m, 5H, Ar-H) (NH too broad to be observed).

Due to the sensitive nature of Mannich base **13**, the material was used immediately without further purification.

(*N*-Benzamidopyrrol-2-ylmethyl)trimethylammonium iodide (14)

2-Dimethylaminomethyl-*N*-benzamidopyrrole (1.00 g, 4.1 mmol) in absolute ethanol (10 mL) was cooled to 0 °C and a solution of iodomethane (0.32 mL, 1.25 eq., 5.13 mmol) in absolute ethanol (5 mL) was slowly added dropwise. After the addition was complete, the mixture was stirred vigorously for 2 h and allowed to warm to room temperature for 2 h and then placed in the freezer overnight. Diethyl ether (25 mL) was then added and the solid product filtered off and recrystallised from diethyl ether to give *(N-benzamidopyrrol-2-ylmethyl)trimethylammonium iodide* (1.58 g, 100%) as a pale yellow solid, mp dec. > 155 °C (Found: C, 46.6; H, 5.5; N, 10.8. $C_{15}H_{20}IN_3O$ requires C, 46.8; H, 5.2; N, 10.9%); ν_{max} (Nujol) 1691, 1671 (C=O) cm^{-1}; δ_H (CD_3OD) 3.22 (s, 9H, $N^+(CH_3)_3$), 4.51 (s, 2H, $CH_2N^+(CH_3)_3$), 6.48 (d, 1H, 3-H), 6.73 (t, 1H, 4-H), 7.17 (d, 1H, 5-H), 7.70–7.79 and 8.09–8.17 (m, 5H, Ar-H) (NH too broad to be observed); *m/z* 258 (M^+, 46%) and 199 (100).

General procedure for attempted base catalysed generation of dipoles 7 and 15 from quaternary salts 6 and 14

The appropriate base (DBU, LDA, or ethyldiisopropylamine) (0.5 mmol) was added to a stirred suspension of the quaternary salt **6** or **14** (0.5 mmol) and the appropriate dipolarophile (1.0 mmol) in the anhydrous solvent (THF, MeCN or DMSO) (2 mL). Stirring was continued at the desired temperature (rt or reflux) for 4 h under a positive flow of dry nitrogen and periodically monitored by TLC [SiO_2, ethyl acetate–hexane (1 : 1)]. The reactions were then quenched with saturated aqueous ammonium chloride (10 mL), and extracted with ethyl acetate (3 × 5 mL). The combined organic fractions were washed with water, brine and dried over anhydrous $MgSO_4$. The solvents were removed *in vacuo* and the residue examined by ^1H NMR ($CDCl_3$). In no cases were any characterisable products of intramolecular cycloaddition obtained.

(4*R*)-1,3-Thiazolidine-4-carboxylic acid (17, R = H)[2]

L-Cysteine (7.6 g, 62.7 mmol) was dissolved in water (20 mL) and formaldehyde (5 mL, 40% aq. soln., 67 mmol) added. The mixture was stirred overnight at room temperature and then cooled in ice for 2 h. The reaction mixture was then filtered and the filter-cake washed thoroughly with *cold* water to give *(4R)-1,3-thiazolidine-4-carboxylic acid* (6.2 g, 74%) as colourless needles, mp 197–198 °C, lit.[2] 196–197 °C (Found: C, 36.2; H, 5.3; N, 10.5. $C_4H_7NO_2S$ requires C, 36.1; H, 5.3; N, 10.5%);

ν_{max} (Nujol) 1628 (C=O) cm^{-1}; *m/z* 133 (M^+, 26%), 88 (100) and 61 (73). Accurate mass: 133.0196, $C_4H_7NO_2S$ requires 133.0197.

General procedure for the preparation of 2-substituted (4*R*)-1,3-thiazolidine-4-carboxylic acids

L-Cysteine (5.60 g, 0.046 mol) was suspended in distilled water (25 mL) and cooled to ~0 °C. To the stirring mixture was added the appropriate pre-cooled aldehyde (0.05 mol) and the flask stoppered to prevent escape of the volatile reagent. After 1 h of stirring at ~0 °C, the reaction mixture was filtered, diluted with absolute alcohol (250 mL) and left in the fridge for a few hours. The resulting mass of crystals was broken up with a spatula and allowed to stand overnight in the fridge. The product was then filtered off and washed thoroughly with diethyl ether. The product was collected by filtration and dried on the vacuum line to give the desired 2-substituted-(4*R*)-1,3-thiazolidine-4-carboxylic acid.

(4*R*)-2-Methylthiazolidine-4-carboxylic acid (17, R = Me).[12] Colourless solid (4.21 g, 62%), mp subl. 138–139 °C, dec. 167 °C, lit.[12] subl. >140 °C, dec. 166–168 °C (Found: C, 40.7; H, 6.2; N, 9.5. Calc. for $C_5H_9NO_2S$: C, 40.8; H, 6.2; N, 9.5%); ν_{max} (Nujol) 1612 (C=O) cm^{-1}; δ_H (D_2O) 1.64–1.67 (m, 3H, 2-CH_3), 3.43 (m, 2H, CH_2), 4.30 (t, 1H, *J* 6 Hz, H-4) and 4.96 (br q, 1H, *J* 7 Hz, H-2); *m/z* 147 (M^+, 24%), 132 (100), 102 (71), 86 (63), 75 (11) and 55 (53). Accurate mass: 147.03495, $C_5H_9NSO_2$ requires 147.0340.

(4*R*)-2-Phenyl-1,3-thiazolidine-4-carboxylic acid (17, R = Ph).[13] Colourless solid (6.47 g, 67%), mp 158–159 °C lit.[13] 159–160 °C (Found: C, 57.5; H, 5.2; N, 6.5. Calc. for $C_{10}H_{11}NO_2S$: C, 57.4; H, 5.3; N, 6.7%); ν_{max} (Nujol) 1575 (C=O) cm^{-1}; *m/z* 209 (M^+, 12%), 164 (34), 137 (100), 117 (89), 104 (56), 77 (30) and 59 (23). Accurate mass: 209.0511, $C_{10}H_{11}NSO_2$ requires 209.0511.

(4*R*)-2-(4-Methoxyphenyl)-1,3-thiazolidine-4-carboxylic acid (17, R = 4-MeOC_6H_4). Colourless solid (8.29 g, 75%), mp 207–208 °C (Found: C, 55.2; H, 5.5; N, 5.9. $C_{11}H_{13}NO_3S$ requires C, 55.2; H, 5.4; N, 5.9%); ν_{max} (Nujol) 1578 (C=O) cm^{-1}; *m/z* 239 (M^+, 19%), 134 (100), 77 (30).

(4*R*)-2-(2-Thienyl)-1,3-thiazolidine-4-carboxylic acid (17, R = 2-thienyl).[14] Colourless solid (9.34 g, 94%), mp dec. 146–147 °C, lit.[14] 145–146 °C (Found: C, 44.5; H, 4.2; N, 6.5. Calc. for $C_8H_9NO_2S_2$: C, 44.6; H, 4.2; N, 6.5%); ν_{max} (Nujol) 1580 (C=O) cm^{-1}.

General procedure for the preparation of dimethyl 3-substituted-5-methyl-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazole-6,7-dicarboxylates

The appropriate 2-substituted-(4*R*)-thiazolidine-4-carboxylic acid (40 mmol) and dimethyl acetylenedicarboxylate (7.4 mL, 1.5 eq., 60 mmol) were dissolved in acetic anhydride (40 mL) and the mixture heated at reflux for three hours under a positive flow of dry nitrogen. The reaction was cooled to room temperature and the solvent removed *in vacuo* to give a brown crystalline mass which was recrystallised from methanol to give the desired dimethyl 3-substituted-5-methyl-1*H*,3*H*-pyrrolo-[1,2-*c*][1,3]thiazole-6,7-dicarboxylate.

Dimethyl 5-methyl-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazole-6,7-dicarboxylate (19, R = H).[2] Cream coloured needles (5.6 g, 55%), mp 133 °C, lit.[2] 131–132 °C (Found: C, 51.8; H, 5.1; N, 5.5. Calc. for $C_{11}H_{13}NO_4S$: C, 51.8; H, 5.1; N, 5.5%); ν_{max} (Nujol) 1718 and 1703 (C=O) cm^{-1}; δ_H ($CDCl_3$) 2.37 (s, 3H, 5-CH_3), 3.80 (s, 3H, ester CH_3), 3.84 (s, 3H, ester CH_3), 4.27 (s, 2H, 1,1-H) and 4.92 (s, 2H, 3,3-H); δ_C ($CDCl_3$) 11.5 (CH_3), 30.2 (CH_2), 47.4 (CH_2), 51.3 (CH_3), 51.5 (CH_3), 107.1, 116.6, 130.5, 139.7, 164.0 (C=O ester) and 165.3 (C=O ester); *m/z* 255 (M^+, 24%), 223 (100), 178 (41), 165 (37) and 137 (42). Accurate mass: 255.0565, $C_{11}H_{13}NO_4S$ requires 255.0565.

Dimethyl 3,5-dimethyl-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazole-6,7-dicarboxylate (19, R = Me). Light brown solid (4.3 g, 40%), mp 112–114 °C (Found: C, 53.2; H, 4.4; N, 4.0. $C_{12}H_{15}NO_4S$ requires C, 53.4; H, 4.5; N, 4.2%); ν_{max} (Nujol) 1737 and 1699 (C=O) cm^{-1}; δ_H ($CDCl_3$) 1.72 (d, 3H, *J* 6 Hz, 3-CH_3), 2.39 (s, 3H, 5-CH_3), 3.79 (s, 3H, ester CH_3), 3.84 (s, 3H, CH_3), 4.18 (d, 1H, *J* 15 Hz, 1-H), 4.34 (d, 1H, *J* 15 Hz, 1-H) and 5.38 (q, 1H, *J* 6 Hz, 3-H).

Dimethyl 5-methyl-3-phenyl-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]-thiazole-6,7-dicarboxylate (19, R = Ph).[13] Light brown solid (9.0 g, 68%), mp 164–165 °C, lit.[13] 163–165 °C (Found: C, 46.0; H, 4.6; N, 4.9. Calc. for $C_{17}H_{17}NO_4S$: C, 46.1; H, 4.6; N, 4.9%); ν_{max} (Nujol) 1728 and 1703 (C=O) cm^{-1}; δ_H ($CDCl_3$) 2.01 (s, 3H, 5-CH_3), 3.83 (s, 6H, ester CH_3), 4.32 (d, 1H, *J* 15 Hz, 1-H), 4.48 (d, 1H, *J* 15 Hz, 1-H), 6.29 (s, 1H, 3-H), 7.05–7.08 and 7.34–7.37 (m, 5H, Ar-H); δ_C ($CDCl_3$) 11.4 (CH_3), 30.0 (CH_2), 51.4 (CH_3 ester), 51.5 (CH_3 ester), 65.0 (CH), 106.9, 117.5, 125.7 (2 × CH), 129.1 (CH), 129.3 (2 × CH), 130.8, 140.2, 140.6, 164.1 (C=O ester) and 165.4 (C=O ester); *m/z* 331 (M^+, 18%), 299 (58), 210 (19), 178 (41), 121 (100), 77 (21).

Dimethyl 3-(4-methoxyphenyl)-5-methyl-1*H*,3*H*-pyrrolo-[1,2-*c*][1,3]thiazole-6,7-dicarboxylate (19, R = 4-MeOC_6H_4). Light brown solid (8.23 g, 57%), mp 166–168 °C (Found: C, 59.6; H, 5.2; N, 3.7. $C_{18}H_{19}NO_5S$ requires C, 59.8; H, 5.3; N, 3.9%); ν_{max} (Nujol) 1730 and 1692 (C=O) cm^{-1}; δ_H ($CDCl_3$) 2.00 (s, 3H, 5-CH_3), 3.80 (s, 3H, $C_6H_4OCH_3$), 3.83 (s, 6H, ester CH_3), 4.30 (d, 1H, *J* 15 Hz, 1-H), 4.48 (d, 1H, *J* 15 Hz, 1-H), 6.27 (s, 1H, 3-H), 6.86 (d, 2H, *J* 7 Hz, Ar-H) and 7.03 (d, 2H, *J* 7 Hz, Ar-H); *m/z* 361 (M^+, 9%), 329 (16), 151 (100).

Dimethyl 5-methyl-3-(2-thienyl)-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]-thiazole-6,7-dicarboxylate (19, R = 2-thienyl). Light brown solid (5.39 g, 40%), mp 148–150 °C (Found: C, 53.2; H, 4.4; N, 4.0. $C_{15}H_{15}NO_4S_2$ requires C, 53.4; H, 4.5; N, 4.2%); ν_{max} (Nujol) 1730 and 1705 (C=O) cm^{-1}; δ_H ($CDCl_3$) 2.14 (s, 3H, 5-CH_3), 3.83 (s, 6H, ester CH_3), 4.31 (d, 1H, *J* 15 Hz, 1-H), 4.50 (d, 1H, *J* 15 Hz, 1-H), 6.57 (s, 1H, 3-H), 6.89–6.93 and 7.30–7.34 (m, 3H, Ar-H); δ_C ($CDCl_3$) 11.2 (CH_3), 29.9 (CH_2), 51.4 (CH_3 ester), 51.5 (CH_3 ester), 60.6 (CH), 107.0, 117.0, 125.7 (CH), 126.8 (CH), 127.1 (CH), 130.8, 139.7, 144.1, 164.0 (C=O ester) and 165.5 (C=O ester); *m/z* 337 (M^+, 23%), 305 (46), 210 (42), 178 (46), 128 (100) and 127 (85). Accurate mass: 337.0444, $C_{15}H_{15}NO_4S_2$ requires 337.0443.

General procedure for the preparation of dimethyl 2,2-dioxo-3-substituted-5-methyl-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazole-6,7-dicarboxylates

3-Chloroperoxybenzoic acid (90%) (1.65 g, 2.2 eq., 9.6 mmol) was added portionwise to a vigorously stirring solution of the appropriate dimethyl 3-substituted 5-methyl-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazole-6,7-dicarboxylate (1.0 g, 3.9 mmol) in dichloromethane (50 mL) at 0 °C. After 1 h, the cooling bath was removed and the reaction mixture was allowed to warm to room temperature. After stirring at room temperature for 3 h, the reaction mixture was washed twice with 10% (w/v) aqueous sodium metabisulfite solution (2 × 100 mL) and twice with 10% (w/v) aqueous $NaHCO_3$ solution (2 × 100 mL). The combined organic fractions were then washed with water (100 mL), brine (100 mL) and dried over anhydrous $MgSO_4$. Concentration *in vacuo* gave colourless crystals which crystallised from methanol to give the desired dimethyl 3-substituted-5-methyl-2,2-dioxo-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazole-6,7-dicarboxylate.

Dimethyl 2,2-dioxo-5-methyl-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazole-6,7-dicarboxylate (20, R = H).[2] Cream coloured needles (1.1 g, 99%), mp 166 °C, lit.[2] 166–167 °C (Found: C, 46.0; H, 4.6; N, 4.9. Calc. for $C_{11}H_{13}NO_6S$: C, 46.1; H, 4.6; N, 4.9%); ν_{max} (Nujol) 1718 and 1701 (C=O) cm^{-1}; δ_H ($CDCl_3$) 2.40 (s, 3H, 5-CH_3), 3.82 (s, 3H, ester CH_3), 3.85 (s, 3H, ester CH_3), 4.57 (s, 2H, 1,1-H) and 4.88 (s, 2H, 3,3-H); δ_C ($CDCl_3$) 11.6 (CH_3), 51.7 (CH_3), 51.8 (CH_3), 52.9 (CH_2), 64.0 (CH_2), 112.4, 115.5, 127.7, 133.0, 163.0 (C=O ester) and 164.6 (C=O ester); *m*/*z* 287 (M^+, 8%), 223 (100).

Dimethyl 2,2-dioxo-3,5-dimethyl-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]-thiazole-6,7-dicarboxylate (20, R = Me). Colourless crystals (1.1 g, 95%), mp 160–162 °C (Found: C, 47.6; H, 5.1; N, 4.7. $C_{12}H_{15}NO_6S$ requires C, 47.8; H, 5.0; N, 4.7%); ν_{max} (Nujol) 1713 and 1697 (C=O) cm^{-1}; δ_H ($CDCl_3$) 1.74 (d, 3H, *J* 7 Hz, 3-CH_3), 2.44 (s, 3H, 5-CH_3), 3.82 (s, 3H, ester CH_3), 3.86 (s, 3H, ester CH_3), 4.35 (d, 1H, *J* 17 Hz, 1-H), 4.66 (d, 1H, *J* 17 Hz, 1-H) and 4.96 (q, 1H, *J* 7 Hz, 3-H); δ_C ($CDCl_3$) 11.3 (CH_3), 17.5 (CH_3), 50.3 (CH_2), 51.7 (CH_3 ester), 51.8 (CH_3 ester), 70.5 (CH), 112.2, 115.8, 126.5, 132.7, 163.2 (C=O ester) and 164.9 (C=O ester); *m*/*z* 301 (M^+, 17%), 237 (93), 205 (100), 119 (45) and 77 (33). Accurate mass: 301.0623, $C_{12}H_{15}NO_6S$ requires 301.0620.

Dimethyl 2,2-dioxo-5-methyl-3-phenyl-1*H*,3*H*-pyrrolo[1,2-*c*]-[1,3]thiazole-6,7-dicarboxylate (20, R = Ph). Yellowish needles (1.34 g, 94%), mp 174–176 °C (Found: C, 56.1; H, 4.6; N, 3.7. $C_{17}H_{17}NO_6S$ requires C, 56.2; H, 4.7; N, 3.9%); ν_{max} (Nujol) 1728 and 1701 (C=O) cm^{-1}; δ_H ($CDCl_3$) 2.16 (s, 3H, 5-CH_3), 3.86 (s, 3H, ester CH_3), 3.87 (s, 3H, ester CH_3), 4.39 (d, 1H, *J* 16 Hz, 1-H), 4.71 (d, 1H, *J* 16 Hz, 1-H), 6.29 (s, 1H, 3-H), 7.02–7.04 and 7.45–7.48 (m, 5H, Ar-H); δ_C ($CDCl_3$) 11.4 (CH_3), 50.4 (CH_2), 51.8 (CH_3 ester), 77.9 (CH), 112.3, 116.0, 127.0 (2 × CH), 127.5, 129.7 (CH), 129.9, 130.9 (2 × CH), 133.7, 163.2 (C=O ester) and 164.8 (C=O ester); *m*/*z* 363 (M^+, 2%), 299 (8), 267 (57), 266 (100), 181 (24), 77 (11). Accurate mass: 363.0781, $C_{17}H_{17}NO_6S$ requires 363.0776.

Dimethyl 2,2-dioxo-3-(4-methoxyphenyl)-5-methyl-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazole-6,7-dicarboxylate (20, R = 4-MeO-C_6H_4). Colourless powder (1.36 g, 95%), mp 179–181 °C (Found: C, 54.7; H, 4.9; N, 3.4. $C_{18}H_{19}NO_7S$ requires C, 55.0; H, 4.8; N, 3.6%); ν_{max} (Nujol) 1709 (C=O) cm^{-1}; δ_H ($CDCl_3$) 2.15 (s, 3H, 5-CH_3), 3.83 (s, 3H, $C_6H_4OCH_3$), 3.86 (s, 3H, ester CH_3), 3.87 (s, 3H, ester CH_3), 4.39 (d, 1H, *J* 17 Hz, 1-H), 4.69 (d, 1H, *J* 17 Hz, 1-H), 5.86 (s, 1H, 3-H), 6.87 (d, 2H, *J* 7 Hz, Ar-H) and 7.04 (d, 2H, *J* 7 Hz, Ar-H); δ_C ($CDCl_3$) 11.4 (CH_3), 50.2 (CH_2), 51.8 (2 × CH_3 ester), 55.4 (CH_3 ether), 77.8 (CH), 112.2, 115.2 (2 × CH), 116.0, 121.5, 127.5, 128.6 (2 × CH), 133.7, 161.6, 163.2 (C=O ester) and 164.8 (C=O ester); *m*/*z* 393 (M^+, 2%), 329 (38), 296 (79), 266 (100), 211 (57), 149 (34).

Dimethyl 2,2-dioxo-5-methyl-3-(2-thienyl)-1*H*,3*H*-pyrrolo-[1,2-*c*][1,3]thiazole-6,7-dicarboxylate (20, R = 2-thienyl). Colourless crystals (1.42 g, 98%), mp 149–151 °C (Found: C, 48.9; H, 4.1; N, 3.8. $C_{15}H_{15}NO_6S_2$ requires C, 48.8; H, 4.1; N, 3.8%); ν_{max} (Nujol) 1714 and 1696 (C=O) cm^{-1}; δ_H ($CDCl_3$) 2.24 (s, 3H, 5-CH_3), 3.85 (s, 3H, ester CH_3), 3.86 (s, 3H, ester CH_3), 4.46 (d, 1H, *J* 16 Hz, 1-H), 4.72 (d, 1H, *J* 16 Hz, 1-H), 6.13 (s, 1H, 3-H), 7.01–7.05, 7.10–7.13 and 7.49–7.51 (m, 3H, Ar-H); δ_C ($CDCl_3$) 11.3 (CH_3), 49.8 (CH_2), 51.9 (CH_3 ester), 74.0 (CH), 112.1, 118.0, 127.0, 128.3 (CH), 129.1 (CH), 129.3 (CH), 132.4, 133.9, 161.5 (C=O ester) and 162.2 (C=O ester); *m*/*z* 369 (M^+, 2%), 305 (36), 272 (100), 187 (30).

Dimethyl 2,2-dioxo-1,5-dimethyl-1*H*,3*H*-pyrrolo[1,2-*c*]-[1,3]thiazole-6,7-dicarboxylate (22)

LiHMDS (3.48 mL, 1.0 M in hexanes, 3.48 mmol) was slowly added to a solution of dimethyl 2,2-dioxo-5-methyl-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazole-6,7-dicarboxylate (1.0 g, 3.48 mmol) in anhydrous THF (60 mL) at −78 °C and the mixture stirred for 1 h. A solution of iodomethane (0.27 mL, 1.25 eq., 4.34 mmol) was then added slowly dropwise *via* cannula and the reaction mixture stirred for a 1 h. The reaction mixture was then allowed to warm to room temperature and quenched with saturated aqueous ammonium chloride solution (200 mL). The organics were extracted with ethyl acetate (3 × 100 mL), washed with water (100 mL), brine (100 mL) and dried over anhydrous $MgSO_4$. The solvent was removed *in vacuo* and the crude residue recrystallised from methanol to give *dimethyl 2,2-dioxo-1,5-dimethyl-1H,3H-pyrrolo[1,2-c][1,3]thiazole-6,7-dicarboxylate* (1.0 g, 95%) as yellowish needles, mp 104–106 °C (Found: C, 47.6; H, 4.9; N, 4.7. $C_{12}H_{15}NO_6S$ requires C, 47.8; H, 5.0; N, 4.7%); ν_{max} (Nujol) 1719 and 1701 (C=O) cm^{-1}; δ_H ($CDCl_3$) 1.66 (d, 3H, *J* 7 Hz, 1-CH_3), 2.38 (s, 3H, 5-CH_3), 3.83 (s, 3H, ester CH_3), 3.85 (s, 3H, ester CH_3), 4.59 (q, 1H, *J* 7 Hz, 1-H), 4.79 (d, 1H, *J* 11 Hz, 3-H) and 4.91 (d, 1H, *J* 11 Hz, 3-H); δ_C ($CDCl_3$) 11.4 (CH_3), 15.3 (CH_3), 51.7 (CH_3 ester), 51.8 (CH_3 ester), 58.0 (CH), 61.9 (CH_2), 112.2, 115.4, 132.6, 133.5, 163.3 (C=O ester) and 164.8 (C=O ester); *m*/*z* 301 (M^+, 3%), 237 (28), 205 (100), 147 (54), 119 (74). Accurate mass: 301.0620, $C_{12}H_{15}NO_6S$ requires 301.0620.

Dimethyl 2,2-dioxo-1,1,5-trimethyl-1*H*,3*H*-pyrrolo[1,2-*c*]-[1,3]thiazole-6,7-dicarboxylate (23)

LiHMDS (3.48 mL, 1.0 M in hexanes, 3.48 mmol) was slowly added to a solution of dimethyl 2,2-dioxo-5-methyl-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazole-6,7-dicarboxylate (1.0 g, 3.48 mmol) in anhydrous THF (60 mL) at −78 °C and the mixture stirred for 1 h. A solution of iodomethane (0.27 mL, 1.25 eq., 4.34 mmol) was then added slowly dropwise *via* cannula and the reaction mixture allowed to warm to room temperature. After stirring for one hour the reaction mixture was recooled to −78 °C and LiHMDS (3.48 mL, 3.48 mmol) added. After stirring for 1 h at −78 °C, a second solution of iodomethane (0.27 mL, 1.25 eq., 4.34 mmol) in anhydrous THF (5 mL) was added, and the resulting solution allowed to warm to room temperature. The reaction mixture was quenched with saturated aqueous ammonium chloride solution (200 mL) and the organics were extracted with ethyl acetate (3 × 100 mL), washed with water (100 mL), brine (100 mL) and dried over anhydrous $MgSO_4$. The solvent was removed *in vacuo* and the crude residue recrystallised from methanol to give *dimethyl 2,2-dioxo-1,1,5-trimethyl-1H,3H-pyrrolo[1,2-c][1,3]thiazole-6,7-dicarboxylate* (1.08 g, 98%) as colourless needles, mp 149–150 °C (Found: C, 49.4; H, 5.4; N, 4.4. $C_{13}H_{17}NO_6S$ requires C, 49.5; H, 5.4; N, 4.4%); ν_{max} (Nujol) 730 and 1696 (C=O) cm^{-1}; δ_H ($CDCl_3$) 1.74 (s, 6H, 1,1-CH_3), 2.40 (s, 3H, 5-CH_3), 3.82 (s, 3H, ester CH_3), 3.85 (s, 3H, ester CH_3) and 4.83 (s, 2H, 3,3-H); δ_C ($CDCl_3$) 11.4 (CH_3), 21.0 (2 × CH_3), 51.7 (CH_3 ester), 51.9 (CH_3 ester), 60.5, 62.3 (CH_2), 112,5, 114.9, 132.0, 135.2, 164.4 (C=O ester) and 164.7 (C=O ester); *m*/*z* 315 (M^+, 4%), 251 (21), 219 (100) and 133 (66). Accurate mass: 315.0776, $C_{13}H_{17}NO_6S$ requires 315.0777.

Pyrolysis of dimethyl 3,5-dimethyl-2,2-dioxo-1*H*,3*H*-pyrrolo-[1,2-*c*][1,3]thiazole-6,7-dicarboxylate (20, R = Me)

Flash pyrolysis of dimethyl 3,5-dimethyl-2,2-dioxo-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazole-6,7-dicarboxylate (0.2 g, 0.7 mmol) at 600 °C/1 × 10^{-3} Torr onto a surface cooled at −196 °C over 2 h gave a yellowish pyrolysate. The pyrolysate was warmed to room temperature under a positive flow of dry nitrogen and removed from the cold finger with dichloromethane. The solvent was removed *in vacuo* and the residue purified by flash chromatography [SiO_2, ethyl acetate–petroleum ether (1 : 1)] to give *dimethyl 2,5-dimethyl-1-vinyl-1H-pyrrole-3,4-dicarboxylate* **25** (0.11 g, 70%) as a yellowish oil (Found: C, 60.6; H, 6.1; N,

5.7. $C_{12}H_{15}NO_4$ requires C, 60.8; H, 6.3; N, 5.9%); ν_{max} (neat) 1700 (C=O) cm^{-1}; δ_H ($CDCl_3$) 2.37 (s, 6H, 2,5-CH_3), 3.81 (s, 6H, 2 × ester CH_3), 5.28 (d, 1H, *J* 15 Hz, CH_2=CH), 5.43 (d, 1H, *J* 8 Hz, CH_2=CH), and 6.61 (dd, 1H, *J* 15, 8 Hz, CH_2=C*H*); *m*/*z* 237 (M^+, 36%), 205 (100), 147 (39), 119 (77). Accurate mass: 237.1001, $C_{12}H_{15}NO_4$ requires 237.1001.

Pyrolysis of dimethyl 1,5-dimethyl-2,2-dioxo-1*H*,3*H*-pyrrolo-[1,2-*c*][1,3]thiazole-6,7-dicarboxylate (22)

Flash pyrolysis of dimethyl 1,5-dimethyl-2,2-dioxo-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazole-6,7-dicarboxylate (0.2 g, 0.7 mmol) at 600 °C/1 × 10^{-3} Torr onto a surface cooled at −196 °C over 2 h gave a yellowish pyrolysate. The pyrolysate was allowed to warm to room temperature under a positive flow of dry nitrogen and removed from the cold finger with dichloromethane. The solvent was removed *in vacuo* and the residue, which showed 3 bands on TLC, was purified by flash chromatography [SiO_2, ethyl acetate–petroleum ether (1 : 1)]. The main band was a yellowish oil which contained *dimethyl 1,2-dimethyl-5-vinyl-1H-pyrrole-3,4-dicarboxylate* **27** as the major component. δ_H ($CDCl_3$) 2.45 (s, 3H, 2-CH_3), 3.81 (s, 3H, ester CH_3), 3.82 (s, 3H, ester CH_3), 5.42 (dd, 1H, *J* 12, 2 Hz, CH_2=CH), 5.53 (dd, 1H, 17, *J* 2 Hz, CH_2=CH) and 6.66 (dd, 1H, *J* 12, 17 Hz, CH_2=C*H*); *m*/*z* 237 (M^+, 30%), 205 (58), 173 (100), 119 (54). Accurate mass: 237.0998, $C_{12}H_{15}NO_4$ requires 237.1001. This fraction was insufficiently pure for complete characterisation and attempts to identify minor impurities in this fraction using liquid chromatography–mass spectrometry (LCMS) were unsuccessful.

Pyrolysis of dimethyl 2,2-dioxo-1,1,5-trimethyl-1*H*,3*H*-pyrrolo-[1,2-*c*][1,3]thiazole-6,7-dicarboxylate (23)

Pyrolysis of dimethyl 2,2-dioxo-1,1,5-trimethyl-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazole-6,7-dicarboxylate (0.2 g, 0.6 mmol) at 600 °C/1 × 10^{-3} Torr onto a surface cooled at −196 °C over 2 h gave a yellowish pyrolysate. The pyrolysate was warmed to room temperature, under a positive flow of dry nitrogen and removed from the cold finger with dichloromethane. The solvent was removed *in vacuo* and the residue purified by flash chromatography [SiO_2, ethyl acetate–petroleum ether (1 : 1)] to give *dimethyl 2-isopropenyl-1,5-dimethyl-1H-pyrrole-3,4-dicarboxylate* **29** (0.12 g, 76%) as a yellowish oil (Found: C, 61.9; H, 6.6; N, 5.3. $C_{13}H_{17}NO_4$ requires C, 62.2; H, 6.8; N, 5.6%); ν_{max} (Nujol) 1721 and 1694 (C=O) cm^{-1}; δ_H ($CDCl_3$) 2.01 (s, 3H, CH_2=C(CH_3)–), 2.42 (s, 3H, 5-CH_3), 3.41 (s, 3H, 1-CH_3), 3.77 (s, 3H, ester CH_3), 3.79 (s, 3H, ester CH_3), 5.03 (s, 1H, CH_2=C(CH_3)–) and 5.42 (s, 1H, CH_2=C(CH_3)–); *m*/*z* 251 (M^+, 55%), 219 (100), 187 (52), 133 (75), 56 (45). Accurate mass: 251.1154, $C_{13}H_{17}NO_4$ requires 251.1158.

General procedure for the preparation of dimethyl 1-acyl-2,2-dioxo-5-methyl-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazole-6,7-dicarboxylates

LiHMDS (3.48 mL, 1.0 M in hexanes, 3.48 mmol) was slowly added to a solution of dimethyl 2,2-dioxo-5-methyl-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazole-6,7-dicarboxylate (1.0 g, 3.48 mmol) in anhydrous THF (60 mL) at −78 °C and the mixture stirred for 30 min. To the reaction mixture was added a solution of the appropriate acyl chloride (2.61 mmol, 0.75 eq.) in anhydrous THF (5 mL) *via* cannula and the mixture was allowed to warm to room temperature. After stirring for 1 h the reaction mixture was recooled to −78 °C and LiHMDS (3.48 mL, 3.48 mmol) added. After stirring for 30 min at −78 °C, a second portion of the appropriate acyl chloride (2.61 mmol, 0.75 eq.) in anhydrous THF (5 mL) was added and the resulting solution allowed to warm to room temperature. After stirring for 1 h the reaction mixture was quenched with saturated aqueous ammonium chloride solution (200 mL) and extracted with ethyl acetate (3 × 100 mL). The combined organic fractions were then thoroughly washed with water (100 mL) and brine (100 mL) and dried over anhydrous $MgSO_4$. Removal of the solvent *in vacuo* gave a dark oil which was purified by column chromatography [SiO_2, ethyl acetate–petroleum ether (1 : 1)] to give the desired dimethyl 1-acyl-2,2-dioxo-5-methyl-1*H*,3*H*-pyrrolo-[1,2-*c*][1,3]thiazole-6,7-dicarboxylate.

Dimethyl 1-benzoyl-2,2-dioxo-5-methyl-1*H*,3*H*-pyrrolo[1,2-*c*]-[1,3]thiazole-6,7-dicarboxylate (30, R = Ph). Colourless crystals (0.94 g, 69%), mp 221–222 °C (Found: C, 54.9; H, 4.1; N, 3.7. $C_{18}H_{17}NO_7S$ requires C, 55.2; H, 4.3; N, 3.6%); ν_{max} (Nujol) 1730, 1714 and 1687 (C=O) cm^{-1}; δ_H ($CDCl_3$) 2.47 (s, 3H, 5-CH_3), 3.58 (s, 3H, ester CH_3), 3.86 (s, 3H, ester CH_3), 4.99 (d, 1H, *J* 11 Hz, 3-H), 5.07 (d, 1H, *J* 11 Hz, 3-H), 6.46 (s, 1H, 1-H), 7.57–7.62, 7.69–7.70 and 8.06–8.09 (m, 5H, Ar-H); δ_C ($CDCl_3$) 11.8 (CH_3), 51.5 (CH_3 ester), 51.8 (CH_3 ester), 63.7 (CH_2), 66.8 (CH), 112.6, 115.4, 129.6 (4 × CH), 129.5, 133.8, 134.9 (CH), 135.4, 162.5 (C=O ester), 164.5 (C=O ester) and 188.8 (C=O ketone); *m*/*z* 391 (M^+, 1%), 327 (2), 105 (100) and 77 (29). Accurate mass: 391.07266, $C_{18}H_{17}NO_7S$ requires 391.07257.

Dimethyl 1-acetyl-2,2-dioxo-5-methyl-1*H*,3*H*-pyrrolo[1,2-*c*]-[1,3]thiazole-6,7-dicarboxylate (30, R = Me). Colourless crystals (0.46 g, 40%), mp 159–160 °C (Found: C, 47.1; H, 4.4; N, 4.2. $C_{13}H_{15}NO_7S$ requires C, 47.4; H, 4.6; N, 4.3%); ν_{max} (KBr) 1719 and 1713 (C=O) cm^{-1}; δ_H ($CDCl_3$) 2.43 (s, 3H, 5-CH_3), 2.54 (s, 3H, COCH_3), 3.80 (s, 3H, ester CH_3), 3.86 (s, 3H, ester CH_3), 4.92 (d, 1H, *J* 11 Hz, 3-H), 4.95 (d, 1H, *J* 11 Hz, 3-H) and 5.57 (s, 1H, 1-H); δ_C ($CDCl_3$) 11.7 (CH_3), 31.4 (CH_3 ketone), 51.8 (2 × CH_3 ester), 63.6 (CH_2), 71.1 (CH), 112.9, 115.4, 129.1, 133.5, 163.0 (C=O ester), 164.4 (C=O ester) and 195.8 (C=O ketone); *m*/*z* 329 (M^+, 5%), 287 (49), 255 (100), 147 (10). Accurate mass: 329.0574, $C_{13}H_{15}NO_7S$ requires 329.0564.

Dimethyl 2,2-dioxo-1-methoxycarbonyl-5-methyl-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazole-6,7-dicarboxylate (30, R = OMe). Colourless crystals (0.46 g, 38%), mp 195–196 °C (Found: C, 45.1; H, 4.2; N, 4.1. $C_{13}H_{15}NO_8S$ requires C, 45.2; H, 4.3; N, 4.1%); ν_{max} (KBr) 1752 and 1715 (C=O) cm^{-1}; δ_H ($CDCl_3$) 2.44 (s, 3H, 5-CH_3), 3.80 (s, 3H, 1-CO_2CH_3), 3.87 (s, 3H, 6-CO_2CH_3), 3.88 (s, 3H, 7-CO_2CH_3), 5.05 (s, 2H, 3,3-H) and 5.40 (s, 1H, 1-H); δ_C ($CDCl_3$) 11.8 (CH_3), 51.8 (CH_3 ester), 51.9 (CH_3 ester), 54.2 (CH_3 ester), 63.5 (CH_2), 67.1 (CH), 113.6, 115.7, 127.5, 133.7, 162.5 (C=O ester), 163.3 (C=O ester) and 164.4 (C=O ester); *m*/*z* 345 (M^+, 14%), 314 (13), 286 (5), 281 (100), 250 (32), 204 (36), 105 (18). Accurate mass: 345.0519, $C_{13}H_{15}NO_8S$ requires 345.0513.

Dimethyl 2,2-dioxo-1-(4-methylbenzoyl)-5-methyl-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazole-6,7-dicarboxylate (30, R = 4-MeC_6H_4). Colourless crystals (1.11 g, 79%), mp 197–198 °C (Found: C, 56.6; H, 4.9; N, 3.6. $C_{19}H_{19}NO_7S$ requires C, 56.3; H, 4.7; N, 3.5%); ν_{max} (KBr) 1737, 1692 and 1655 (C=O) cm^{-1}; δ_H ($CDCl_3$) 2.46 (s, 3H, 5-CH_3), 2.47 (s, 3H, $C_6H_4CH_3$), 3.58 (s, 3H, ester CH_3), 3.86 (s, 3H, ester CH_3), 4.99 (d, 1H, *J* 11 Hz, 3-H), 5.06 (d, 1H, *J* 11 Hz, 3-H), 6.44 (s, 1H, 1-H), 7.39 (d, 2H, *J* 8 Hz, Ar-H), 7.98 (d, 2H, *J* 8 Hz, Ar-H); δ_C ($CDCl_3$) 11.8 (CH_3), 21.9 (CH_3), 51.5 (CH_3 ester), 51.8 (CH_3 ester), 63.6 (CH_2), 66.7 (CH), 112.6, 115.4, 129.4 (2 × CH), 129.6, 130.0 (2 × CH), 133.7, 146.4, 162.5 (C=O ester), 164.5 (C=O ester) and 188.2 (C=O ketone); *m*/*z* 405 (M^+, 1%), 374 (1), 341 (1), 223 (2), 119 (100). Accurate mass: 405.0883, $C_{19}H_{19}NO_7S$ requires 405.0877.

Dimethyl 1-(4-chlorobenzoyl)-2,2-dioxo-5-methyl-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazole-6,7-dicarboxylate (30, R = 4-ClC_6H_4). Colourless crystals (0.59 g, 40%), mp dec. 124–125 °C (Found: C, 50.6; H, 3.5; N, 3.2. $C_{18}H_{16}ClNO_7S$ requires C, 50.8; H, 3.8; N, 3.3%); ν_{max} (KBr) 1735, 1708 and 1687 (C=O) cm^{-1}; δ_H ($CDCl_3$) 2.46 (s, 3H, 5-CH_3), 3.61 (s, 3H, ester CH_3), 3.86 (s,

3H, ester CH_3), 5.00 (d, 1H, *J* 11 Hz, 3-H), 5.05 (d, 1H, *J* 11 Hz, 3-H), 6.40 (s, 1H, 1-H), 7.57 (d, 2H, *J* 10 Hz, Ar-H) and 8.02 (d, 2H, *J* 10 Hz, Ar-H); δ_C ($CDCl_3$) 11.8 (CH_3), 51.6 (CH_3 ester), 51.8 (CH_3 ester), 63.7 (CH_2), 66.9 (CH), 112.8, 115.5, 129.3, 129.7 (2 × CH), 130.6 (2 × CH), 133.7, 133.9, 141.8, 162.7 (C=O ester), 164.5 (C=O ester) and 187.8 (C=O ketone); *m*/*z* 425 (M^+, 2%), 361 (2), 243 (3), 139 (100). Accurate mass: 425.0338, $C_{18}H_{16}ClNO_7S$ requires 425.0331.

Dimethyl 1-(3,4-difluorobenzoyl)-2,2-dioxo-5-methyl-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazole-6,7-dicarboxylate (30, R = 3,4-$F_2C_6H_4$). Yellowish crystals (0.76 g, 51%), mp 152–154 °C (Found: C, 50.4; H, 3.3; N, 3.2. $C_{18}H_{15}F_2NO_7S$ requires C, 50.6; H, 3.5; N, 3.3%); ν_{max} (Nujol) 1740, 1715 and 1693 (C=O) cm^{-1}; δ_H ($CDCl_3$) 2.45 (s, 3H, 5-CH_3), 3.64 (s, 3H, ester CH_3), 3.86 (s, 3H, ester CH_3), 5.02 (s, 2H, 3,3-H), 6.36 (s, 1H, 1-H), 7.35–7.44 and 7.89–7.95 (m, 3H, Ar-H); δ_C ($CDCl_3$) 11.7 (CH_3), 51.7 (CH_3 ester), 51.8 (CH_3 ester), 63.8 (CH_2), 66.9 (CH), 113.0, 115.6, 118.2 (CH), 118.5 (CH), 118.6, 118.8, 126.7, 126.8, 129.2, 133.9 (CH), 163.0 (C=O ester), 164.6 (C=O ester) and 186.8 (C=O ketone); *m*/*z* 427 (M^+, 0.2%), 363 (1), 141 (100), 113 (15). Accurate mass: 427.0531, $C_{18}H_{15}F_2NO_7S$ requires 427.0537.

Dimethyl 1-(2-furoyl)-2,2-dioxo-5-methyl-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazole-6,7-dicarboxylate (30, R = 2-furyl). Colourless crystals (0.85 g, 64%), mp dec. 210–212 °C (Found: C, 50.4; H, 3.7; N, 3.5. $C_{16}H_{15}NO_8S$ requires C, 50.4; H, 3.9; N, 3.7%); ν_{max} (KBr) 1735, 1715 and 1677 (C=O) cm^{-1}; δ_H ($CDCl_3$) 2.46 (s, 3H, 5-CH_3), 3.64 (s, 3H, ester CH_3), 3.86 (s, 3H, ester CH_3), 4.98 (d, 1H, *J* 11 Hz, 3-H), 5.03 (d, 1H, *J* 11 Hz, 3-H), 6.31 (s, 1H, 1-H), 6.70–6.73 (m, 1H, *J* 2, 5 Hz, Ar-H), 7.50 (d, 1H, *J* 5 Hz, Ar-H) and 7.79 (d, 1H, *J* 2 Hz, Ar-H); δ_C ($CDCl_3$) 11.6 (CH_3), 51.6 (CH_3 ester), 51.8 (CH_3 ester), 63.7 (CH_2), 67.4 (CH), 113.1, 113.8 (CH), 115.5, 120.9 (CH), 128.6, 133.9, 148.9 (CH), 151.4, 162.5 (C=O ester), 164.5 (C=O ester) and 176.3 (C=O ketone); *m*/*z* 381 (M^+, 12%), 317 (100), 285 (28), 199 (34), 81 (32). Accurate mass: 381.0522, $C_{16}H_{15}NO_8S$ requires 381.0513.

Dimethyl 1-cyclohexanoyl-2,2-dioxo-5-methyl-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazole-6,7-dicarboxylate (30, R = cyclohexyl). Colourless needles (1.22 g, 88%), mp 141–142 °C (Found: C, 54.4; H, 5.7; N, 3.5. $C_{18}H_{23}NO_7S$ requires C, 54.4; H, 5.8; N, 3.5%); ν_{max} (KBr) 1721 and 1693 (C=O) cm^{-1}; δ_H ($CDCl_3$) 1.22–1.54, 1.70–1.74, 1.85–1.88, 2.04–2.07 (m, 10H, cyclohexyl ring-H), 2.41 (s, 3H, 5-CH_3), 2.74–2.81 (m, 1H), 3.79 (s, 3H, ester CH_3), 3.85 (ester CH_3), 4.90 (d, 1H, *J* 11 Hz, 3-H), 4.93 (d, 1H, *J* 11 Hz, 3-H) and 5.74 (s, 1H, 1-H); δ_C ($CDCl_3$) 11.7 (CH_3), 25.3 (CH_2), 25.4 (CH_2), 25.6 (CH_2), 27.2 (CH_2), 27.5 (CH_2), 51.7 (CH_3 ester), 51.8 (CH_3 ester), 51.9 (CH), 63.2 (CH_2), 69.0 (CH), 112.5, 115.3, 129.2, 133.4, 163.0 (C=O ester), 164.6 (C=O ester) and 201.4 (C=O ketone); *m*/*z* 397 (M^+, 2%), 366 (2), 333 (1), 255 (15), 111 (45), 83 (100). Accurate mass 397.1199, $C_{18}H_{23}NO_7S$ requires 397.1188.

Dimethyl 7-methyl-3-phenyl-1*H*-pyrrolo[1,2-*c*][1,3]oxazine-5,6-dicarboxylate (32, R = Ph)

Method A (flash pyrolysis). Pyrolysis of dimethyl 1-benzoyl-2,2-dioxo-5-methyl-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazole-6,7-dicarboxylate (0.2 g, 0.5 mmol) at 600 °C/1 × 10^{-3} Torr onto a surface cooled at −196 °C over a 2 h period gave a yellowish pyrolysate. The pyrolysate was allowed to warm to room temperature under a positive flow of dry nitrogen and removed from the cold finger with dichloromethane. The solvent was removed *in vacuo* and the residue purified by flash chromatography [SiO_2, ethyl acetate–petroleum ether (1 : 1)] to give *dimethyl 7-methyl-3-phenyl-1H-pyrrolo[1,2-c][1,3]oxazine-5,6-dicarboxylate* **32** (R = Ph) (0.13 g, 75%) as a yellowish oil (Found: C, 65.8; H, 5.1; N, 4.2. $C_{18}H_{17}NO_5$ requires C, 66.1; H, 5.2; N, 4.3%); ν_{max} (Nujol) 1711 (C=O) cm^{-1}; δ_H ($CDCl_3$) 2.41 (s, 3H, 7-CH_3), 3.85 (s, 3H, ester CH_3), 3.86 (s, 3H, ester CH_3), 5.66 (s, 2H, CH_2), 6.96 (s, 1H, CH), 7.33–7.44 and 7.68–7.71 (m, 5H, Ar-H); δ_C ($CDCl_3$) 10.0 (CH_3), 51.4 (CH_3 ester), 51.5 (CH_3 ester), 72.9 (CH_2), 95.2 (CH), 108.6, 114.6, 124.9 (2 × CH), 128.5 (2 × CH), 129.5 (CH), 130.8, 132.4, 152.1, 164.6 (C=O ester) and 165.5 (C=O ester); *m*/*z* 327 (M^+, 60%), 295 (35), 237 (20), 209 (100), 105 (57), 77 (58). Accurate mass: 327.1106, $C_{18}H_{17}NO_5$ requires 327.1107.

Method B (solution pyrolysis). A suspension of dimethyl 1-benzoyl-2,2-dioxo-5-methyl-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazole-6,7-dicarboxylate (0.2 g, 0.5 mmol) in 1,2,4-trichlorobenzene (2 mL) was heated at reflux under dry nitrogen for 4 h. After cooling to room temperature the mixture was purified by flash chromatography [SiO_2, petroleum ether] to remove the 1,2,4-trichlorobenzene followed by elution with [ethyl acetate–petroleum ether (1 : 1)] to yield pure *dimethyl 7-methyl-3-phenyl-1H-pyrrolo[1,2-c][1,3]oxazine-5,6-dicarboxylate* (0.14 g, 86%) as a yellowish oil, which had identical physical and spectral properties to the product isolated in method A.

General procedure for the preparation of dimethyl 3-substituted-7-methyl-1*H*-pyrrolo[1,2-*c*][1,3]oxazine-5,6-dicarboxylates

Using method B (solution pyrolysis) described above the following pyrrolo[1,2-*c*]oxazines were obtained:

Dimethyl 3,7-dimethyl-1*H*-pyrrolo[1,2-*c*][1,3]oxazine-5,6-dicarboxylate (32, R = Me). Yellowish oil (0.1 g, 52%) (Found: C, 58.7; H, 5.8; N, 5.3. $C_{13}H_{15}NO_5$ requires C, 58.9; H, 5.7; N, 5.3%); δ_H ($CDCl_3$) 2.00 (s, 3H, 3-CH_3), 2.35 (s, 3H, 7-CH_3), 3.81 (s, 3H, ester CH_3), 3.83 (s, 3H, ester CH_3), 5.48 (s, 2H, CH_2) and 6.20 (s, 1H, CH); δ_C ($CDCl_3$) 9.9 (CH_3), 19.0 (CH_3), 51.2 (CH_3 ester), 51.5 (CH_3 ester), 72.4 (CH_2), 96.5 (CH), 113.4, 117.0, 130.0, 130.9, 153.7, 162.2 (C=O ester) and 162.9 (C=O ester); *m*/*z* 265 (M^+, 59%), 233 (65), 175 (50), 147 (100) and 43 (27). Accurate mass: 265.0951, $C_{13}H_{15}NO_5$ requires 265.0950.

Dimethyl 7-methyl-3-(4-methylphenyl)-1*H*-pyrrolo[1,2-*c*][1,3]-oxazine-5,6-dicarboxylate (32, R = 4-MeC_6H_4). Yellowish solid (0.14 g, 85%), mp 108–110 °C (Found: C, 66.5; H, 5.8; N, 4.3. $C_{19}H_{19}NO_5$ requires C, 66.8; H, 5.6; N, 4.1%); ν_{max} (KBr) 1711 and 1693 (C=O) cm^{-1}; δ_H ($CDCl_3$) 2.38 (s, 3H, $C_6H_4CH_3$), 2.41 (s, 3H, 7-CH_3), 3.85 (s, 3H, ester CH_3), 3.86 (s, 3H, ester CH_3), 5.65 (s, 2H, CH_2), 6.92 (s, 1H, CH), 7.21 (d, 2H, *J* 12 Hz, Ar-H) and 7.59 (d, 2H, *J* 12 Hz, Ar-H); δ_C ($CDCl_3$) 10.0 (CH_3), 21.4 (CH_3), 51.4 (CH_3 ester), 51.6 (CH_3 ester), 72.8 (CH_2), 94.4 (CH), 108.2, 114.4, 124.9 (2 × CH), 129.3 (2 × CH), 129.6, 130.6, 131.1, 139.8, 152.4, 164.7 (C=O ester) and 165.6 (C=O ester); *m*/*z* 341 (M^+, 100%), 310 (21), 223 (57), 105 (31). Accurate mass: 341.1267, $C_{19}H_{19}NO_5$ requires 341.1257.

Dimethyl 3-(4-chlorophenyl)-7-methyl-1*H*-pyrrolo[1,2-*c*][1,3]-oxazine-5,6-dicarboxylate (32, R = 4-ClC_6H_4). Yellowish solid (0.13 g, 76%), mp dec. 130–132 °C (Found: C, 59.7; H, 4.6; N, 4.1. $C_{18}H_{16}ClNO_5$ requires C, 59.8; H, 4.4; N, 3.9%); ν_{max} (KBr) 1719 and 1699 (C=O) cm^{-1}; δ_H ($CDCl_3$) 2.41 (s, 3H, 7-CH_3), 3.85 (s, 3H, ester CH_3), 3.86 (s, 3H, ester CH_3), 5.66 (s, 2H, CH_2), 6.94 (s, 1H, CH), 7.36 (d, 2H, *J* 10 Hz, Ar-H) and 7.62 (d, 2H, *J* 10 Hz, Ar-H); δ_C ($CDCl_3$) 10.0 (CH_3), 51.6 (CH_3 ester), 51.8 (CH_3 ester), 72.9 (CH_2), 95.5 (CH), 108.9, 114.6, 126.1 (2 × CH), 128.9 (2 × CH), 130.8, 131.8, 131.9, 135.3, 150.9, 164.6 (C=O ester) and 165.5 (C=O ester); *m*/*z* 361 (M^+, 100%), 329 (42), 271 (19), 243 (77), 139 (24). Accurate mass: 361.0713, $C_{18}H_{16}ClNO_5$ requires 361.0713.

Dimethyl 3-(3,4-difluorophenyl)-7-methyl-1*H*-pyrrolo[1,2-*c*]-[1,3]oxazine-5,6-dicarboxylate (32, R = 3,4-$F_2C_6H_4$). Yellowish oil (0.1 g, 60%) (Found: C, 59.3; H, 3.9; N, 3.6. $C_{18}H_{15}F_2NO_5$ requires C, 59.5; H, 4.1; N, 3.9%); δ_H ($CDCl_3$) 2.41 (s, 3H,

7-CH_3), 3.85 (s, 3H, ester CH_3), 3.86 (s, 3H, ester CH_3), 5.66 (s, 2H, CH_2), 6.90 (s, 1H, CH), 7.14–7.23 and 7.41–.53 (m, 3H, Ar-H); δ_C ($CDCl_3$) 10.0 (CH_3), 51.5 (CH_3 ester), 51.6 (CH_3 ester), 73.0 (CH_2), 96.0 (CH), 109.6, 114.1 (CH), 114.4, 117.6 (CH), 121.2 (CH), 127.0, 129.9, 130.2, 131.0, 140.1, 149.9, 164.3 (C=O ester) and 165.5 (C=O ester); *m/z* 363 (M^+, 56%), 331 (43), 245 (100), 141 (48), 113 (47). Accurate mass: 363.0905, $C_{18}H_{15}F_2NO_5$ requires 363.0918.

Dimethyl 3-(2-furyl)-7-methyl-1*H*-pyrrolo[1,2-*c*][1,3]oxazine-5,6-dicarboxylate (32, R = 2-furyl). Yellowish–orange solid (0.12 g, 72%), mp dec. 113–115 °C (Found: C, 60.4; H, 4.5; N, 4.1. $C_{16}H_{15}NO_6$ requires C, 60.4; H, 4.7; N, 4.4%); ν_{max} (KBr) 1710 and 1697 (C=O) cm^{-1}; δ_H ($CDCl_3$) 2.40 (s, 3H, 7-CH_3), 3.84 (s, 3H, ester CH_3), 3.86 (s, 3H, CH_3), 5.60 (s, 2H, CH_2), 6.46–6.48 (m, 1H, *J* 3, 5 Hz, Ar-H), 6.64 (d, 1H, *J* 5 Hz, Ar-H), 6.84 (s, 1H, CH) and 7.47 (d, 1H, *J* 3 Hz, Ar-H); δ_C ($CDCl_3$) 10.0 (CH_3), 51.4 (CH_3 ester), 51.6 (CH_3 ester), 72.8 (CH_2), 94.4 (CH), 109.0, 109.3 (CH), 111.8 (CH), 114.6, 130.2, 131.1, 143.8 (CH), 144.3, 147.6, 164.4 (C=O ester) and 165.5 (C=O ester); *m/z* 317 (M^+, 100%), 286 (23), 199 (50), 81 (40). Accurate mass: 317.0916, $C_{16}H_{15}NO_6$ requires 317.0894.

Dimethyl 3-cyclohexyl-7-methyl-1*H*-pyrrolo[1,2-*c*][1,3]-oxazine-5,6-dicarboxylate (32, R = cyclohexyl). Colourless solid (0.11, 68%), mp 112–114 °C (Found: C, 64.7; H, 6.8; N, 4.3. $C_{18}H_{23}NO_5$ requires C, 64.9; H, 6.9; N, 4.2%); ν_{max} (Nujol) 1713 and 1690 (C=O) cm^{-1}; δ_H ($CDCl_3$) 1.16–1.34, 1.68–1.88, 2.13–2.17 (m, 11H, cyclohexyl ring-H), 2.35 (s, 3H, 7-CH_3), 3.81 (s, 3H, ester CH_3), 3.82 (s, 3H, ester CH_3), 5.45 (s, 2H, N-CH_2-O) and 6.17 (s, 1H, 4-H); δ_C ($CDCl_3$) 9.9 (CH_3), 25.9 (CH_2), 30.2 (CH_2), 41.6 (CH), 51.2 (CH_3 ester), 51.5 (CH_3 ester), 72.6 (CH_2), 94.0 (CH), 107.0, 112.0, 130.2, 131.1, 161.7, 164.6 (C=O ester) and 165.5 (C=O ester); *m/z* 333 (M^+, 82%), 301 (92), 243 (32), 215 (100) and 55 (36). Accurate mass: 333.1577 $C_{18}H_{23}NO_5$ requires 333.1576.

Dimethyl 2,2-dioxo-1*H*,3*H*-pyrazolo[1,5-*c*][1,3]thiazole-6,7-dicarboxylate (35)

3-Chloroperoxybenzoic acid (90%) (1.65 g, 2.2 eq., 9.6 mmol) was added portionwise to a vigorously stirring solution of dimethyl 1*H*,3*H*-pyrazolo[1,5-*c*][1,3]thiazole-6,7-dicarboxylate[6] (0.95 g, 3.92 mmol) in dichloromethane (50 mL) at 0 °C. After 1 h, the cooling bath was removed and the reaction mixture was allowed to warm to room temperature. After stirring at room temperature for 3 h, the reaction mixture was washed twice with 10% (w/v) aqueous sodium metabisulfite solution (2 × 100 mL) and twice with 10% (w/v) aqueous $NaHCO_3$ (2 × 100 mL). The combined organic fractions were then washed with water (100 mL), brine (100 mL) and dried over anhydrous $MgSO_4$. Concentration *in vacuo* gave colourless crystals which crystallised from methanol to give *dimethyl 2,2-dioxo-1H,3H-pyrazolo[1,5-c][1,3]thiazole-6,7-dicarboxylate* (1.05 g, 98%) as colourless needles, mp 138–140 °C (Found: C, 39.5; H, 3.7; N, 10.2. $C_9H_{10}N_2O_6S$ requires C, 39.4; H, 3.7; N, 10.2%); ν_{max} (Nujol) 1732 (C=O) cm^{-1}; δ_H ($CDCl_3$) 3.87 (s, 3H, ester CH_3), 3.97 (s, 3H, ester CH_3), 4.69 (t, 2H, *J* 2 Hz, 1-CH_2) and 5.25 (t, 2H, *J* 2 Hz, 3-CH_2); δ_C ($CDCl_3$) 52.4 (CH_3), 53.0 (CH_3), 53.4 (CH_2), 67.29 (CH_2), 111.9, 139.6, 146.5, 160.9 (C=O ester) and 161.3 (C=O ester); *m/z* 274 (M^+, 1%), 210 (67), 151 (100), 64 (18) and 59 (28).

Dimethyl 5,6-bis(trimethylsilyl)-4,7-dihydropyrazolo-[1,5-*a*]pyridine-2,3-dicarboxylate (37)

Method A (sealed-tube). Dimethyl 2,2-dioxo-1*H*,3*H*-pyrazolo[1,5-*c*][1,3]thiazole-6,7-dicarboxylate (0.1 g, 0.4 mmol) was suspended in toluene (2 mL) in a glass pyrolysis tube with bis(trimethylsilyl)acetylene (0.18 mL, 2 eq., 0.8 mmol). The tube was then cooled in liquid nitrogen, evacuated, sealed and placed in a pre-heated oven at 300 °C. After 3 h the tube was removed, cooled to room temperature and carefully reopened. The reaction mixture was filtered and the solvent removed *in vacuo* to give a dark residue. Purification by flash chromatography [SiO_2, ethyl acetate–hexane (1 : 1)] gave *dimethyl 5,6-bis(trimethylsilyl)-4,7-dihydropyrazolo[1,5-a]pyridine-2,3-dicarboxylate* (0.028 g, 20%) as a yellowish oil (Found: C, 54.0; H, 7.5; N, 7.4. $C_{17}H_{28}N_2O_4Si_2$ requires C, 53.7; H, 7.4; N, 7.4%); ν_{max} (neat) 1745 (C=O) cm^{-1}; δ_H ($CDCl_3$) 0.24 (s, 9H, Si(CH_3)$_3$), 0.26 (s, 9H, Si(CH_3)$_3$), 3.75 (t, 2H, *J* 5 Hz, CH_2), 3.82 (s, 3H, ester CH_3), 3.92 (s, 3H, ester CH_3) and 4.73 (t, 2H, *J* 5 Hz, CH_2); *m/z* 380 (M^+, 6%), 365 (19), 348 (29), 275 (87), 203 (16), 73 (100). Accurate mass: 380.1578, $C_{17}H_{28}N_2O_4Si_2$ requires 380.1588.

Method B (solution pyrolysis). A suspension of dimethyl 2,2-dioxo-1*H*,3*H*-pyrazolo[1,5-*c*][1,3]thiazole-6,7-dicarboxylate (0.1 g, 0.4 mmol) in 1,2,4-trichlorobenzene (2 mL) was heated at reflux with bis(trimethylsilyl)acetylene (0.18 mL, 2 eq., 0.8 mmol) under dry nitrogen for 3 h. After cooling to room temperature the mixture was purified by flash chromatography [SiO_2, petroleum ether] to remove the 1,2,4-trichlorobenzene followed by elution with ethyl acetate–petroleum ether (1 : 1) to yield *dimethyl 5,6-bis(trimethylsilyl)-4,7-dihydropyrazolo-[1,5-a]pyridine-2,3-dicarboxylate* (0.033 g, 24%) as a yellowish oil which had identical physical and spectral properties to the compound prepared by method A.

Dimethyl 5,6-bis(trimethylsilyl)pyrazolo[1,5-*a*]pyridine-2,3-dicarboxylate (38)

Method A (sealed-tube). Dimethyl 2,2-dioxo-1*H*,3*H*-pyrazolo[1,5-*c*][1,3]thiazole-6,7-dicarboxylate (0.1 g, 0.4 mmol) was suspended in toluene (2 mL) in a glass pyrolysis tube with bis(trimethylsilyl)acetylene (0.18 mL, 2 eq., 0.8 mmol). The tube was then cooled in liquid nitrogen, evacuated, sealed and placed in a pre-heated oven at 300 °C. After 6 h the tube was removed, cooled to room temperature and carefully reopened. The reaction mixture was filtered and the solvent removed *in vacuo* to give a dark residue. Purification by flash chromatography [SiO_2, ethyl acetate–hexane (1 : 1)] gave *dimethyl 5,6-bis(trimethylsilyl)pyrazolo[1,5-a]pyridine-2,3-dicarboxylate* (0.033 g, 24%) as a yellowish oil (Found: C, 54.0; H, 7.1; N, 7.5. $C_{17}H_{26}N_2O_4Si_2$ requires C, 54.0; H, 6.9; N, 7.4%); ν_{max} (neat) 1749 and 1713 (C=O) cm^{-1}; δ_H ($CDCl_3$) 0.42 (s, 9H, Si(CH_3)$_3$), 0.43 (s, 9H, Si(CH_3)$_3$), 3.94 (s, 3H, ester CH_3), 4.03 (s, 3H, ester CH_3), 8.45 (s, 1H, Ar-H) and 8.59 (s, 1H, Ar-H); *m/z* 378 (M^+, 100%), 363 (26), 347 (52), 331 (91), 259 (50), 158 (33), 73 (77). Accurate mass: 378.1435, $C_{17}H_{26}N_2O_4Si_2$ requires 378.1431.

Method B (solution pyrolysis). A suspension of dimethyl 2,2-dioxo-1*H*,3*H*-pyrazolo[1,5-*c*][1,3]thiazole-6,7-dicarboxylate (0.1 g, 0.4 mmol) in 1,2,4-trichlorobenzene (2 mL) was heated at reflux with bis(trimethylsilyl)acetylene (0.18 mL, 2 eq., 0.8 mmol) under dry nitrogen for 6 h. After cooling to room temperature the mixture was purified by flash chromatography [SiO_2, petroleum ether] to remove the 1,2,4-trichlorobenzene followed by elution with ethyl acetate–petroleum ether (1 : 1) to yield *dimethyl 5,6-bis(trimethylsilyl)pyrazolo[1,5-a]pyridine-2,3-dicarboxylate* (0.028 g, 20%) as a yellowish oil which had identical physical and spectral properties to the compound prepared by method A.

Dimethyl 5-trimethylsilylpyrazolo[1,5-*a*]pyridine-2,3-dicarboxylate (39) and dimethyl 6-trimethylsilylpyrazolo[1,5-*a*]-pyridine-2,3-dicarboxylate (40)

Dimethyl 2,2-dioxo-1*H*,3*H*-pyrazolo[1,5-*c*][1,3]thiazole-6,7-dicarboxylate (0.1 g, 0.4 mmol) was suspended in toluene

(2 mL) in a glass pyrolysis tube with trimethylsilylacetylene (0.11 mL, 2 eq., 0.8 mmol). The tube was then cooled in liquid nitrogen, evacuated, sealed and placed in a pre-heated oven at 300 °C. After 4 h the tube was removed, cooled to room temperature and carefully reopened. The reaction mixture was filtered and the solvent removed *in vacuo* to give a dark residue. Purification by flash chromatography [SiO_2, ethyl acetate–hexane (1 : 1)] gave *dimethyl 6-trimethylsilylpyrazolo[1,5-a]-pyridine-2,3-dicarboxylate* **40** (0.01 g, 9%) as a yellowish oil (Found: C, 54.6; H, 5.7; N, 9.0. $C_{14}H_{18}N_2O_4Si$ requires C, 54.9; H, 5.9; N, 9.2%); ν_{max} (neat) 1730 (C=O) cm^{-1}; δ_H ($CDCl_3$) 0.34 (s, 9H, Si(CH_3)$_3$), 3.92 (s, 3H, ester CH_3), 4.03 (s, 3H, ester CH_3), 7.47 (d, 1H, *J* 9 Hz, Ar-H), 8.14 (d, 1H, *J* 9 Hz, Ar-H) and 8.50 (s, 1H, Ar-H); *m*/*z* 306 (M^+, 70%), 291 (100), 275 (42), 201 (16). Accurate mass: 306.1038, $C_{14}H_{18}N_2O_4Si$ requires 306.1036, and *dimethyl 5-trimethylsilylpyrazolo[1,5-a]pyridine-2,3-dicarboxylate* **39** (0.01 g, 9%) as a yellowish oil (Found: C, 54.5; H, 5.7; N, 9.1. $C_{14}H_{18}N_2O_4Si$ requires C, 54.9; H, 5.9; N, 9.2%); ν_{max} (neat) 1729 (C=O) cm^{-1}; δ_H ($CDCl_3$) 0.36 (s, 9H, Si(CH_3)$_3$), 3.94 (s, 3H, ester, CH_3), 4.03 (s, 3H, ester CH_3), 7.11 (d, 1H, *J* 7 Hz, Ar-H), 8.30 (s, 1H, Ar-H) and 8.50 (d, 1H, *J* 7 Hz, Ar-H); *m*/*z* 306 (M^+, 99%), 291 (36), 275 (61), 259 (100), 201 (12). Accurate mass: 306.1038, $C_{14}H_{18}N_2O_4Si$ requires 306.1036.

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References

1 O. B. Sutcliffe, R. C. Storr, T. L Gilchrist, P. Rafferty and A. P. A. Crew, *Chem. Commun.*, 2000, 675.
2 A. Padwa, G. E. Fryxell, J. R. Gasdaska, K. Venkatramanan and G. S. K. Wong, *J. Org. Chem.*, 1989, **54**, 644.
3 S. J. Collier and R. C. Storr, *Prog. Heterocycl. Chem.*, 1998, **10**, 25.
4 (*a*) J. Bergman and R. Carlsson, *Tetrahedron Lett.*, 1977, 4663; (*b*) S. Kano, E. Sugino, S. Shibuya and S. Hibino, *J. Org. Chem.*, 1981, **46**, 2979; (*c*) S. Kano, N. Mochizuki, S. Hibino and S. Shibuya, *J. Org. Chem.*, 1982, **47**, 3566; (*d*) P. M. S. Chauhan, G. Jenkins, S. Walker and R. C. Storr, *Tetrahedron Lett.*, 1988, **117**, 5.
5 H. Shimoharada, S. Ikeda, S. Kajigaeshi and S. Kanemasa, *Chem. Lett.*, 1977, 1237.
6 O. B. Sutcliffe, R. C. Storr, T. L. Gilchrist and P. Rafferty, *Tetrahedron*, 2000, 10011.
7 J. Sauer, D. K. Heldmann, J. Hetzenegger, J. Krauthan, H. Sichert and J. Schuster, *Eur. J. Org. Chem.*, 1998, 2885.
8 T. Sasaki, K. Kanematsu and A. Kakehi, *J. Org. Chem.*, 1971, **36**, 2978; K. T. Potts, H. P. Youzwak and S. J. Zurawel, *J. Org. Chem.*, 1980, **45**, 90.
9 (*a*) M. J. S. Dewar and W. Thiel, *J. Am. Chem. Soc.*, 1977, **99**, 4899; (*b*) J. P. Stewart, *J. Comput. Chem.*, 1989, **10**, 209.
10 (*a*) C. W. Jefford and W. Johncock, *Helv. Chim. Acta*, 1983, **66**, 2666; (*b*) C. Kashima, T. Maruyama, K. Harada, S. Hibi and Y. Omote, *J. Chem. Res. (M)*, 1988, 601.
11 W. Flitsch, U. Kramer and H. Zimmermann, *Chem. Ber.*, 1969, **102**, 3268.
12 H. T. Nagasawa, D. J. W. Goon, W. P. Muldoon and R. T. Zera, *J. Med. Chem.*, 1984, **27**, 591.
13 Z. Györgydeák, L. Szilágyi, K. J. Kajtár, G. Argay and A. Kálmán, *Monatsh. Chem.*, 1994, **125**, 189.
14 H. Soloway, F. Kipnis, J. Ornfelt and P. E. Spoerri, *J. Am. Chem. Soc.*, 1948, **70**, 1667.