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'Higher-order' azomethine ylides in the synthesis of functionalized pyrroles and 5-oxo-5*H*-pyrrolizines

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Abstract—Azafulvenium methides generated by the thermal extrusion of SO_2 from 1-methyl- and 1,1-dimethyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-2,2-dioxides undergo [1,8]H sigmatropic shifts to give vinylpyrroles. Flash vacuum pyrolysis of the *C*-vinylpyrroles affords 5-oxo-5*H*-pyrrolizines or *C*-allyl-1*H*-pyrroles.

1. Introduction

Storr and co-workers found that the generation of 1-azafulvenium methides by the thermal extrusion of sulfur dioxide from 1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-2,2-dioxides could be achieved under flash vacuum pyrolysis (FVP) reaction conditions. They described the first evidence for the trapping of these 'higher-order' azomethine ylides in pericyclic reactions. The extended dipolar systems having a methyl group at C-1 or C-7 undergo sigmatropic [1,8]H shifts giving vinylpyrroles and the 1-acyl derivatives electrocyclise to give pyrrolo[1,2-*c*]-[1,3]oxazines.[1] We have further studied the reactivity of azafulvenium methides including the reactivity of a range of new systems derived from 1-unsubstitued-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-2,2-dioxides and showed that these transient 8π 1,7-dipole systems are interesting intermediates for the synthesis of functionalized heterocyclic compounds. The intramolecular trapping of these transient 8π 1,7-dipoles in pericyclic reaction, namely sigmatropic [1,8]H shifts and 1,7-electrocyclization, allowed the synthesis of *N*-vinylpyrroles and *C*-vinylpyrroles, which, under flash vacuum pyrolysis conditions, are converted into 5-oxo-5*H*-pyrrolizines or 4-oxo-1,4-dihydro-1-aza-benzo[*f*]azulenes, respectively. These heterocycles can also be obtained directly by FVP of 1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-2,2-dioxides (Scheme 1).[2]

Here, we report our study on the azafulvenium methides generated from 1-methyl- and 1,1-dimethyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-2,2-dioxides, aiming to get knowledge on the reactivity pattern of these extended dipolar systems. We also intended to evaluate the scope of their use as intermediates in the synthesis of heterocycles.

2. Results and discussion

1,1-Dimethyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-2,2-dioxides **3a**–**3d** were prepared from penicillamine as outlined in Scheme 2. Heating a solution of 5,5-dimethyl-1,3-thiazolidine-4-carboxylic acids **1a**–**1d** in acetic anhydride in the presence of dimethyl acetylenedicarboxylate the corresponding 1,1-dimethyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazoles **2a**–**2d** are obtained in good yield (60–93%) via the intermolecular dipolar cycloaddition of the in situ generated 7,7-dimethyl-3-methyl-5*H*,7*H*-thiazolo[3,4-*c*]oxazol-4-ium-1-olates. Oxidation of 1,1-dimethyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazoles **2a**–**2d** with MCPBA afforded sulfones **3a**–**3d** with yields ranging from 41% to 78%. 1,1-Dimethyl-pyrrolo[1,2-*c*]thiazole-2,2-dioxide **3a** has been prepared before using a less straightforward approach.[1b]

This alkylation procedure[1b] was applied in the synthesis of 1-methyl-pyrrolo[1,2-*c*]thiazole-2,2-dioxide **5** (Scheme 2). The metallation of sulfone **4**[1b] with LiHMDS and subsequent reaction with iodomethane give heterocyclic compound **5** in 82% yield.

Storr and co-workers described that under FVP 1,1-dimethyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-2,2-dioxide **3a** undergoes cheletropic extrusion of sulfur dioxide giving azafulvenium methide **6**, which leads to 2-isopropenylpyrrole **7** via an allowed suprafacial [1,8]H shift in the 8π 1,7-dipolar system.[1b] We observed that the same azafulvenium methide intermediate **6** can also be generated by carrying out thermolysis in a sealed tube and the corresponding pericyclic reaction allows the synthesis of *C*-vinylpyrrole **7**. The

Keywords: Azafulvenium methides; Azomethine ylides; Pyrrolo[1,2-*c*]thiazoles; Pyrroles; 5-Oxo-5*H*-pyrrolizines; Flash vacuum pyrolysis.
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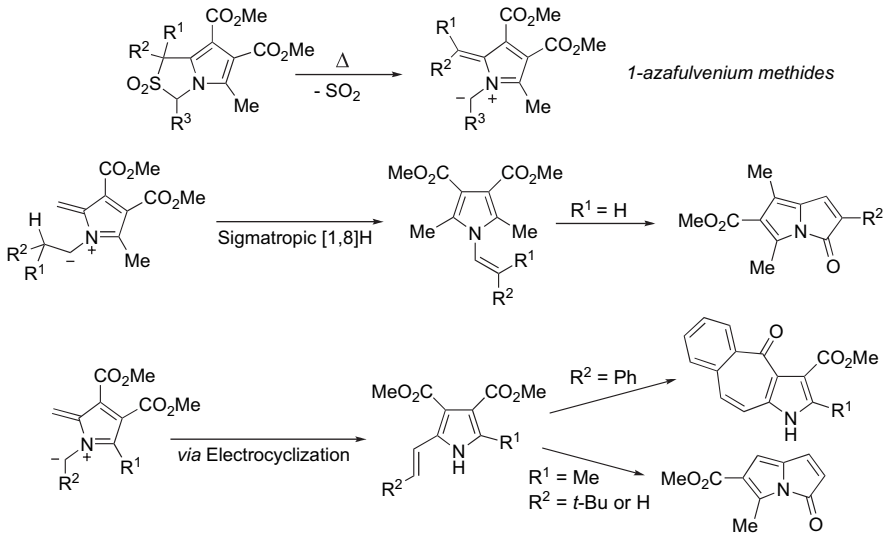
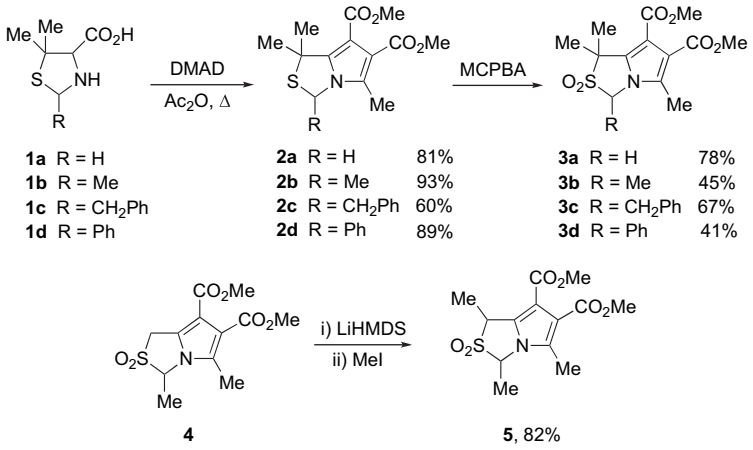


Scheme 1.



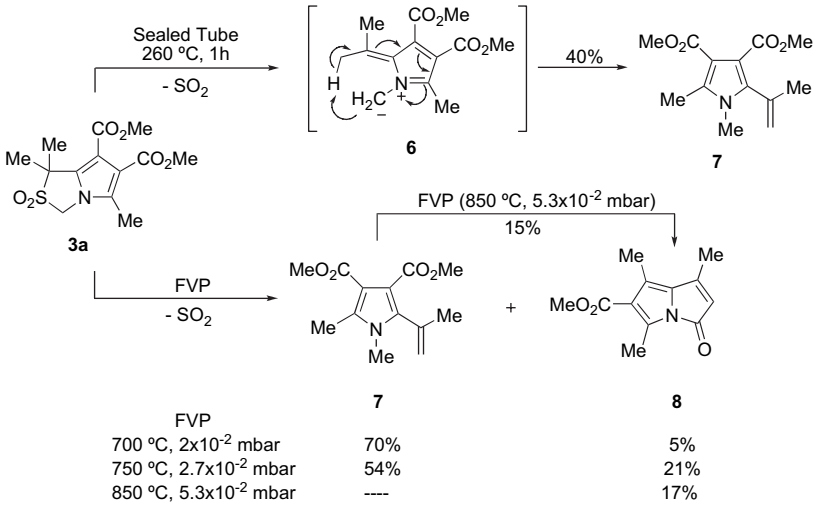
Scheme 2.

best result was obtained by heating at 260 °C for 1 h a solution of **3a** in sulfolane, which gave pyrrole **7** in 40% yield. The FVP of sulfone **3a** under our reaction conditions led to a different outcome than the previously reported result. By carrying out the FVP at 700 °C/2×10^{-2} mbar, the pyrrole **7** was obtained as the major product in 70% yield together with the formation of 5-oxo-5*H*-pyrrolizine **8** in 5% yield. Performing the flash vacuum pyrolysis at 750 °C/2.7×10^{-2} mbar revealed that the pyrrole **7** is again the major product (54%) but 5-oxo-5*H*-pyrrolizine **8** is now obtained in 21% yield. At higher temperature (850 °C/5.3×10^{-2} mbar) only 5-oxo-5*H*-pyrrolizine **8** is obtained although in low yield (Scheme 3).

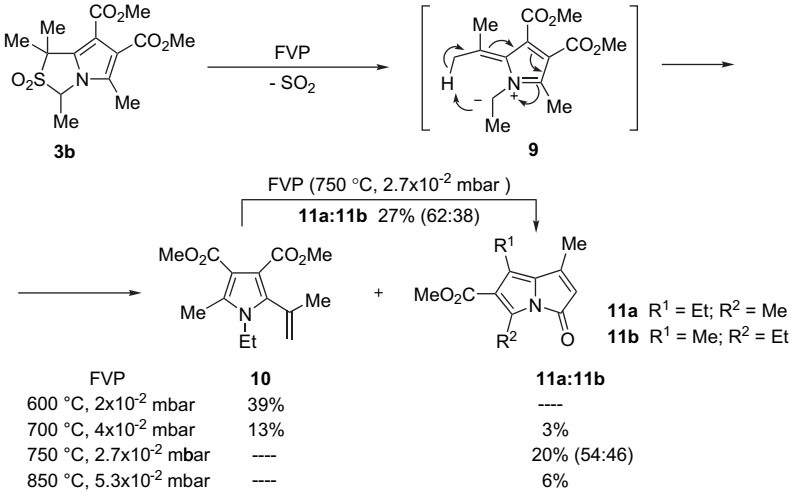
5-Oxo-5*H*-pyrrolizine **8** can also be obtained by the flash vacuum pyrolysis of 2-isopropenylpyrrole **7** (850 °C/4×10^{-2} mbar). This result allowed us to conclude that the 2-isopropenylpyrrole **7** is an intermediate in the synthesis of 5-oxo-5*H*-pyrrolizine **8** from 1,1-dimethyl-pyrrolo[1,2-*c*]-thiazole-2,2-dioxide **3a** (Scheme 3).

The reactivity of 1,1-dimethyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-2,2-dioxide **3b**, bearing an extra methyl group at C-3, was also studied (Scheme 4). In this particular case, the SO_2 extrusion leads to azafulvenium methide **9** where two potential [1,8]H sigmatropic shifts could occur. In fact, it is known that thermolysis of dimethyl 3,5-dimethyl-pyrrolo[1,2-*c*]thiazole-6,7-dicarboxylate-2,2-dioxide can lead to dimethyl 2,5-dimethyl-*N*-vinyl-1*H*-pyrrole-3,4-dicarboxylate via azafulvenium methide **9**.[1,2] However, the flash vacuum pyrolysis of compound **3b** did not afford *N*-vinyl derivatives. Instead, *C*-vinylpyrrole **10** and 5-oxo-5*H*-pyrrolizines **11a** and **11b** were obtained. The FVP conditions determine the outcome of this reaction: at 600 °C/2×10^{-2} mbar the *C*-vinylpyrrole **10** is obtained in moderate yield (39%) whereas at 750 °C/2.7×10^{-2} mbar the FVP affords a mixture of 5-oxo-5*H*-pyrrolizines **11a** and **11b** in 20% yield. These 5-oxo-5*H*-pyrrolizines could also be prepared by the FVP of *C*-vinylpyrrole **10** (Scheme 4). Attempts to carry out the thermolysis of pyrrolo[1,2-*c*]thiazole-2,2-dioxide **3b** in a sealed tube were not successful.

The flash vacuum pyrolysis of 1,1-dimethyl-3-benzyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-2,2-dioxide **3c** leads to the



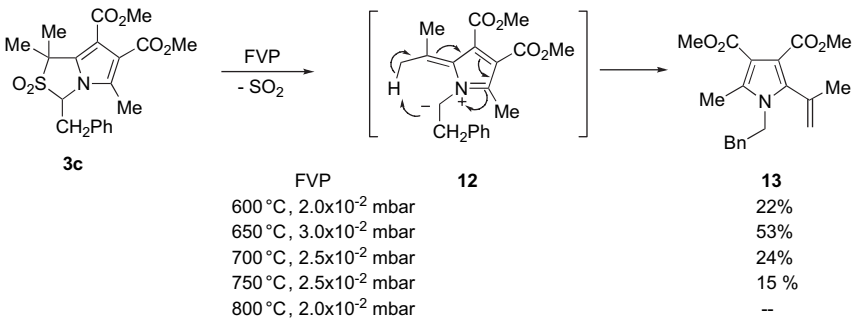
Scheme 3.



Scheme 4.

synthesis of *C*-vinylpyrrole **13** via the [1,8]H shift of azafulvenium methide intermediate **12** (Scheme 5). The best result was obtained by carrying out the FVP at 650 °C/ 3×10^{-2} mbar giving pyrrole **13** in 53% yield.

We observed that the presence of two methyl groups at C-1 in 1,1-dimethyl-3-benzyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-2,2-dioxide **3c** leads to only one reaction channel with the exclusive formation of *C*-vinylpyrrole **13**. Attempts to carry out the thermolysis of 1,1-dimethyl-3-benzyl-1*H*,3*H*-pyrrolo-[1,2-*c*]thiazole-2,2-dioxide **3c** in a sealed tube led to the recovery of the starting material (250 °C, 1.5 h) or to complex mixtures when using more drastic reaction conditions (265 °C, 2.5 h). 5-Oxo-5*H*-pyrrolizines could not be obtained from pyrrole **13** since the volatilization of the starting material, required to perform the FVP, led to significant decomposition of 1,1-dimethyl-3-benzyl-1*H*,3*H*-pyrrolo-[1,2-*c*]thiazole-2,2-dioxide **3c**.



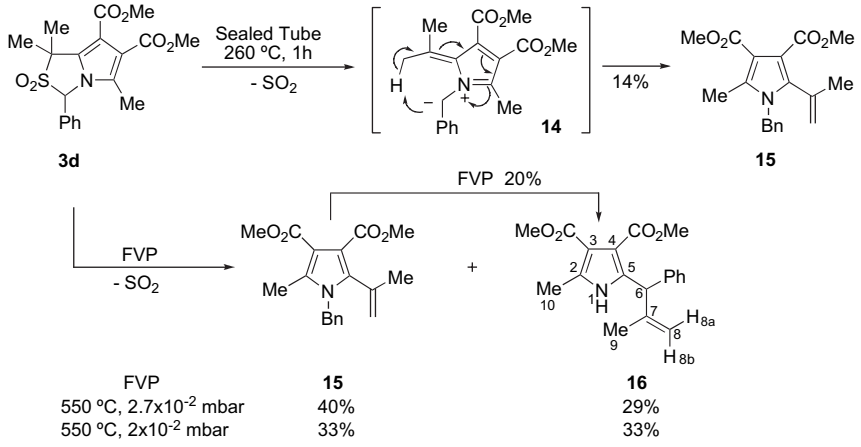
Scheme 5.

1-Benzyl-2-isopropenyl-5-methyl-1*H*-pyrrole-3,4-dicarboxylate **15** was prepared by the thermolysis of sulfone **3d**. This heterocyclic compound is obtained in low yield (14%) by heating a solution of **3d** in sulfolane in a sealed tube at 260 °C for 1 h. The FVP of sulfone **3d** led to the same *C*-vinylpyrrole **15** but an unexpected product **16** was also formed with an overall yield between 66–69%. In this case, it was observed that by carrying out the FVP at higher temperature (700 °C or 850 °C) only traces of the products could be detected. On the other hand, by performing the FVP at lower temperature (450 °C, 2×10^{-2} mbar) no reaction occurs. The FVP of 1-benzyl-2-isopropenyl-5-methyl-1*H*-pyrrole-3,4-dicarboxylate **15** affords 5-(2-methyl-1-phenyl-allyl)-1*H*-pyrrole **16** (20%) proving that pyrrole **15** is an intermediate in the synthesis of compound **16** from sulfone **3d** (Scheme 6).

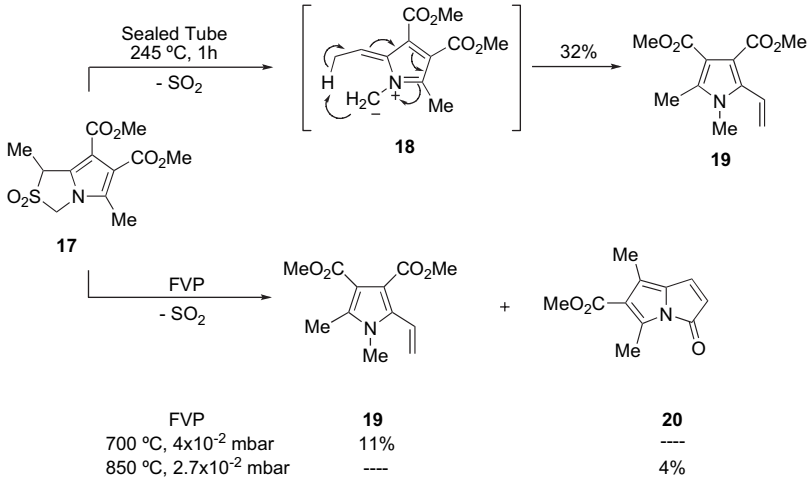
The structural assignment of 1*H*-pyrrole **16** was achieved using two-dimensional NMR techniques. The COSY spectrum showed cross-peaks between H-6 and H-8a, H-8b, H-9 and with the *ortho*-protons of the phenyl group. The spectrum shows also cross-peaks between H-9 and H-8a and H-8b. The HMQC spectrum allowed the assignment of signals corresponding to the side chain carbons with chemical shifts of 22.1 (C-9), 48.8 (C-6) and 113.2 (C-8).

The FVP of 1-methyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-2,2-dioxide **17** to give *C*-vinylpyrrole **19** has been reported although this compound was not obtained pure.[1b] We decided to look again into the chemical behaviour of compound **17**. 1-Methyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-2,2-dioxide **17** was prepared following the synthetic procedure described in the literature.[1b] The SO_2 extrusion of sulfone **17** can be accomplished by sealed tube thermolysis giving pure *C*-vinylpyrrole **19** in 32% yield. The sealed tube thermal reaction carried out at higher temperature (260 °C, 0.75 h) led only to the decomposition of the starting material. The flash vacuum pyrolysis of 1-methyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-2,2-dioxide **17** at 700 °C/4×10^{-2} mbar gave *C*-vinylpyrrole **19** in 11% yield whereas at 850 °C/2.7×10^{-2} mbar methyl 1,3-dimethyl-5-oxo-5*H*-pyrrolizine-2-carboxylate **20** was the sole product (Scheme 7).

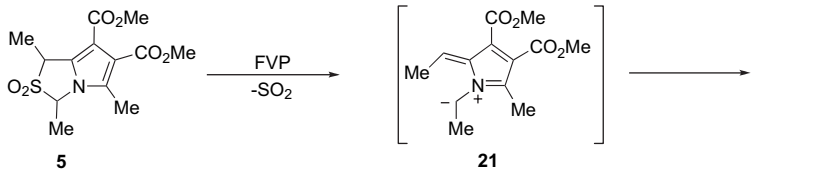
Finally, the reactivity of 1,3-dimethyl-1*H*,3*H*-pyrrolo[1,2-*c*]-thiazole-2,2-dioxide **5** was studied (Scheme 8). This is a case where the SO_2 extrusion leads to an azafulvenium methide, which can undergo two potential [1,8]H sigmatropic shifts. In fact, on FVP the heterocycle **5** participates in both [1,8]H shifts giving the corresponding *C*-vinylpyrrole **23** and *N*-vinylpyrrole **24**. However, these were not the only products and pyrrole **22** was obtained as the major product.



Scheme 6.



Scheme 7.



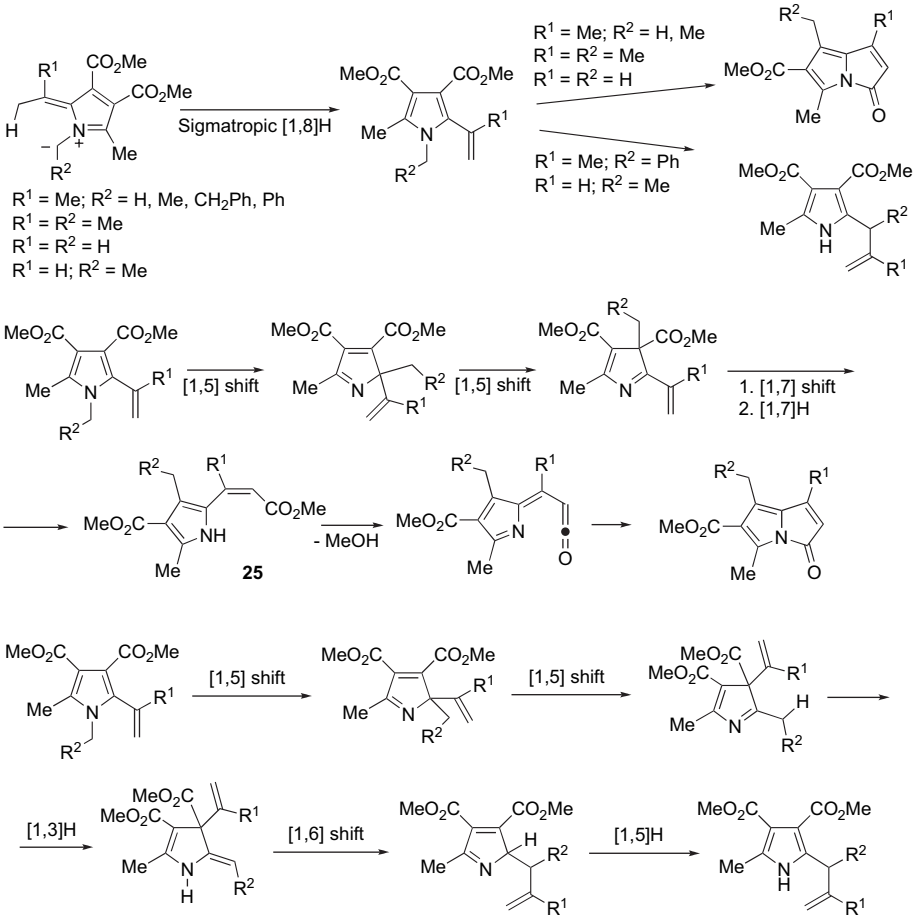
FVP	22	23	24
550 °C, 2.0x10^{-2} mbar*	46%	traces	10%
600 °C, 2.5x10^{-2} mbar	58%	5%	14%
650 °C, 3.0x10^{-2} mbar	39%	10%	13%
700 °C, 3.5x10^{-2} mbar	10%	5%	traces

* **5** = 12%

Scheme 8.

The 2-(but-3-en-2-yl) side chain of pyrrole **22** is easily identified by its ^{1}H NMR spectrum. Three vinylic protons are observed (at 5.12, 5.17 and 5.93–6.04 ppm) together with a multiplet at 4.05–4.10 ppm corresponding to H-2 and a multiplet assigned to the methyl group at 1.33 ppm. On the other hand, the spectrum shows a broad singlet at 8.22 ppm proving that **22** is a *N*-unsubstituted 1*H*-pyrrole. This functionalized pyrrole **22** has a similar substitution pattern to the one of pyrrole **16** (see Scheme 6).

A clear reactivity pattern of the studied azafulvenium methides can be defined (Scheme 9). Azafulvenium methides generated from 1,1-dimethyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-2,2-dioxides undergo [1,8]H sigmatropic shifts to give *C*-vinylpyrroles even in the cases where an alternative pericyclic reactions could in principle occur. Azafulvenium methides generated from a 1-methyl-1*H*,3*H*-pyrrolo[1,2-*c*]-thiazole-2,2-dioxide unsubstituted at C-3 can only undergo the same type of [1,8]H shift to the corresponding



Scheme 9.

C-vinylpyrrole. However, the reaction of 1,3-dimethyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-2,2-dioxide derivative leads to the azafulvenium methide intermediate, which undergoes two possible [1,8]H sigmatropic shifts.

The formation of 5-oxo-5*H*-pyrrolizines from *C*-vinylpyrroles can be rationalized as outlined in Scheme 9. The pyrrol-2-ylpropionates **25** must be intermediates in the synthesis of the 5-oxo-5*H*-pyrrolizines, formed from the *C*-vinylpyrroles through a sequence of sigmatropic shifts. The pyrrol-2-ylpropionates undergo concerted elimination of methanol giving pyrrol-2-ylideneketenes, which are converted into 5-oxo-5*H*-pyrrolizines by electrocyclization. This is in agreement with the reported rearrangement to 5-oxo-5*H*-pyrrolizines.[2,3] The synthesis of **11b** involves an initial methyl migration followed by a sequence of sigmatropic shifts to give the corresponding pyrrol-2-ylpropionates, which is converted to the final product.

The mechanism for the new rearrangement of *C*-vinylpyrroles to give functionalized *C*-allyl-1*H*-pyrroles is shown in Scheme 9.

3. Conclusion

We reported the reactivity of azafulvenium methides generated by the thermal extrusion of sulfur dioxide from 1-methyl- and 1,1-dimethyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-2,2-dioxides as well as the chemical behaviour of *C*-vinylpyrroles towards thermolysis.

Azafulvenium methides generated by thermolysis of 1,1-dimethyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-2,2-dioxides and C-3 unsubstituted 1-methyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-2,2-dioxide undergo [1,8]H sigmatropic shifts to give *C*-vinylpyrroles. However, the thermal reaction of 1-methyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-2,2-dioxide bearing a methyl group at C-3 affords the corresponding *C*-vinylpyrrole and *N*-vinylpyrrole via two competitive [1,8]H sigmatropic shifts. Vinylpyrroles are valuable building blocks for the synthesis of functionalized pyrroles including condensed pyrrole-annulated heterocycles.[3c,4] Moreover, 2-vinylpyrroles are found in many biologically active molecules and they are also of interest as vinyl monomers and as ligands for new photocatalysts and biologically active complexes.[3c,4,5]

Taking advantage of the particular reaction conditions that FVP offers, an important technique for carrying out intramolecular reactions, new *C*-vinylpyrrole rearrangements to afford 5-oxo-5*H*-pyrrolizines or functionalized *C*-allyl-1*H*-pyrroles are also reported. 5-Oxo-5*H*-pyrrolizines are heterocycles with an interesting chemistry, which has been applied to the synthesis of the pyrrolizine alkaloid, 3,8-didehydroheliotridin-5-one.[3b]

4. Experimental

4.1. General

^{1}H NMR spectra were recorded on an instrument operating at 300 MHz or on an instrument operating at 500 MHz. ^{13}C NMR spectra were recorded on an instrument operating at 75.5 MHz or on an instrument operating at 125 MHz. The solvent is deuteriochloroform except where indicated otherwise; chemical shifts are expressed in parts per million related to internal TMS, and coupling constants (*J*) are in hertz. Mass spectra were recorded under electron impact (EI) at 70 eV.

4.2. General procedure for the synthesis of 5,5-dimethyl-1,3-thiazolidine-4-carboxylic acid

DL-Penicillamine (2.98 g, 20 mmol) was dissolved in methanol (400 mL) followed by the dropwise addition of the aldehyde (22 mmol). The reaction mixture was stirred overnight at room temperature. The solvent was evaporated off and the product crystallized.

4.2.1. 5,5-Dimethyl-1,3-thiazolidine-4-carboxylic acid 1a. Yield 84%, mp 200–202 °C (from ethanol) (lit.[6] mp 200–201 °C). IR (KBr) 3010 (br s), 1628, 1382, 1334, 1126 cm^{-1}. ^{1}H NMR (CD_3OD) 1.44 (3H, s), 1.71 (3H, s), 3.77 (1H, s), 4.30 (1H, d, *J*=9.8), 4.38 (1H, d, *J*=9.8).

4.2.2. 2,5,5-Trimethyl-1,3-thiazolidine-4-carboxylic acid 1b. Compound **1b** was obtained as a white solid in 83% yield, mp 192.3–193.2 °C (from ethanol) (lit.[7] mp 186–188 °C). The ^{1}H NMR spectrum showed the presence of two diastereoisomers (ratio 51:49). Major component: ^{1}H NMR (CD_3OD) 1.46 (3H, s), 1.58 (3H, d, *J*=6.3), 1.69 (3H, s), 3.81 (1H, s), 4.76 (1H, q, *J*=6.3). Minor component: ^{1}H NMR (CD_3OD) 1.41 (3H, s), 1.62 (3H, d, *J*=6.4), 1.70 (3H, s), 3.98 (1H, s), 4.96 (1H, q, *J*=6.4). MS (ES^+) *m*/*z* 176 (MH^+, 25%), 159 (100), 130 (46) and 84 (10).

4.2.3. 2-Benzyl-5,5-dimethyl-1,3-thiazolidine-4-carboxylic acid 1c. Compound **1c** was obtained as a white in 70% yield, mp 114–115 °C (from diethyl ether/hexane). IR (KBr) 1638, 1414, 1386, 1117 cm^{-1}. The ^{1}H NMR spectrum showed the presence of two diastereoisomers (ratio 71:29). Major component: ^{1}H NMR 1.22 (3H, s), 1.60 (3H, s), 3.07 (1H, d, *J*=7.5), 3.25 (1H, d, *J*=5.2), 3.81 (1H, s), 4.87 (1H, dd, *J*=5.2 and 7.5), 7.1–7.4 (5H, m, Ar–H). Minor component: ^{1}H NMR 1.35 (3H, s), 1.63 (3H, s), 3.03 (1H, d, *J*=7.5), 3.28 (1H, d, *J*=5.2), 4.12 (1H, s), 5.06 (1H, dd, *J*=5.2 and 7.5), 7.1–7.3 (5H, m, Ar–H). ^{13}C NMR (major component) 28.8, 29.8, 41.9, 56.9, 66.3, 73.8, 127.5, 129.0, 129.7, 136.9, 171.5. Anal. Calcd for $C_{13}H_{17}NO_2S$: C, 62.12; H, 6.82; N, 5.57; S, 12.76%. Found: C, 62.52; H, 7.13; N, 5.93; S, 12.89%.

4.2.4. 5,5-Dimethyl-2-phenyl-1,3-thiazolidine-4-carboxylic acid 1d. Yield 48%, mp 136.7–138.8 °C (from diethyl ether) (lit.[8] mp 145–146 °C, for the thiazolidine obtained from D-penicillamine). The ^{1}H NMR spectrum showed the presence of two diastereoisomers. ^{1}H NMR 1.59 and 1.61 (3H, 2×s), 1.81 and 1.84 (3H, 2×s), 4.08 (1H, s), 6.04 (1H, s), 7.40–7.49 (3H, m, Ar–H), 7.67–7.69 (2H, m, Ar–H).

4.3. General procedure for the synthesis of dimethyl 1,1,5-trimethyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-6,7-dicarboxylates

The appropriate 5,5-dimethyl-1,3-thiazolidine-4-carboxylic acid (5 mmol), dimethyl acetylenedicarboxylate (0.9 mL,

7.5 mmol) and acetic anhydride (20 mL) were heated at 110–120 °C for 4 h. The reaction mixture was cooled to room temperature and was diluted with CH_2Cl_2 (50 mL). The organic phase was washed with a saturated aqueous solution of $NaHCO_3$ and with water, dried ($MgSO_4$) and the solvent was evaporated off. The crude product was purified by flash chromatography (hexane/ethyl acetate).

4.3.1. Dimethyl 1,1,5-trimethyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-6,7-dicarboxylate 2a. Compound **2a** was obtained as a white solid in 81% yield, mp 106.0–107.4 °C (from diethyl ether/hexane). IR (KBr) 1708, 1692, 1530, 1235, 1207 cm^{-1}. ^1H NMR 1.80 (6H, s), 2.34 (3H, s), 3.79 (6H, s), 4.91 (2H, s). ^{13}C NMR 11.0, 30.0, 46.1, 51.4, 51.5, 52.7, 106.4, 116.4, 128.8, 144.3, 164.9, 165.3. MS (EI) *m/z* 283 (M^+, 27%), 268 (23), 252 (11) and 236 (100). Anal. Calcd for $C_{13}H_{17}NO_4S$: C, 55.11; H, 6.05; N, 4.94. Found: C, 55.25; H, 6.26; N, 4.54.

4.3.2. Dimethyl 1,1,3,5-tetramethyl-1*H*,3*H*-pyrrolo[1,2-*c*]-thiazole-6,7-dicarboxylate 2b. Compound **2b** was obtained as a white solid in 93% yield, mp 71.1–72.5 °C (from diethyl ether/hexane). IR (KBr) 1694, 1529, 1232, 1202 cm^{-1}. ^1H NMR 1.72 (3H, s), 1.73 (3H, d, *J*=6.2), 1.88 (3H, s), 2.35 (3H, s), 3.77 (3H, s), 3.79 (3H, s), 5.35 (1H, q, *J*=6.2). MS (EI) *m/z* 297 (M^+, 31%), 282 (28), 266 (9) and 250 (100). Anal. Calcd for $C_{14}H_{19}NO_4S$: C, 56.55; H, 6.44; N, 4.71. Found: C, 56.73; H, 6.63; N, 4.38.

4.3.3. Dimethyl 1,1,5-trimethyl-3-benzyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-6,7-dicarboxylate 2c. Compound **2c** was obtained as a white solid in 60% yield, mp 104–106 °C (from ethyl acetate/hexane). IR (KBr) 1706, 1525, 1228, 1200 cm^{-1}. ^1H NMR 1.63 (3H, s), 1.71 (3H, s), 2.45 (3H, s), 3.16 (1H, dd, *J*=8.7 and 13.8), 3.35 (1H, dd, *J*=3.6 and 13.8), 3.78 (3H, s), 3.82 (3H, s), 5.47 (1H, dd, *J*=3.6 and 8.7), 7.11–7.31 (5H, m, Ar–H). ^{13}C NMR 11.9, 30.6, 32.9, 45.3, 51.9, 52.0, 52.3, 64.2, 106.8, 117.9, 127.8, 129.0, 130.4, 135.4, 145.5, 165.3, 166.0. MS (EI) *m/z* 373 (M^+, 13%), 326 (15), 282 (100), 250 (89) and 206 (27). Anal. Calcd for $C_{20}H_{23}NO_4S$: C, 64.32; H, 6.21; N, 3.75; S, 8.59. Found: C, 64.15; H, 6.17; N, 3.96; S, 8.41.

4.3.4. Dimethyl 1,1,5-trimethyl-3-phenyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-6,7-dicarboxylate 2d. Compound **2d** was obtained as a pale yellow solid in 89% yield, mp 118.6–119.7 °C (from diethyl ether/hexane). IR (KBr) 1705, 1698, 1527, 1227, 1217 cm^{-1}. ^1H NMR 1.84 (3H, s), 1.90 (3H, s), 1.95 (3H, s), 3.81 (3H, s), 3.84 (3H, s), 6.34 (1H, s), 7.06–7.10 (2H, m, Ar–H), 7.33–7.35 (3H, m, Ar–H). MS (EI) *m/z* 359 (M^+, 59%), 344 (64), 312 (100) and 206 (67). Anal. Calcd for $C_{19}H_{21}NO_4S$: C, 63.49; H, 5.89; N, 3.90. Found: C, 63.67; H, 6.30; N, 3.65.

4.4. General procedure for the synthesis of sulfones

To a stirred ice-cold solution of the appropriate dimethyl 1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-6,7-dicarboxylate (1 mmol) in dry dichloromethane (7 mL) was added portionwise 3-chloroperoxybenzoic acid (3 equiv, 3 mmol) under N_2 atmosphere. 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 bisulfite solution (2×20 mL) and twice with 10% (w/v) aqueous sodium bicarbonate solution (2×20 mL). The organic fraction was then dried over anhydrous $MgSO_4$ and the solvent was evaporated off. The crude product was purified by flash chromatography (hexane/ethyl acetate).

4.4.1. Dimethyl 1,1,5-trimethyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-6,7-dicarboxylate-2,2-dioxide 3a. Yield 78%, mp 150.2–151.6 °C (from diethyl ether) (lit.[2b] mp 149–150 °C). MS (EI) *m/z* 315 (M^+, 7%), 284 (12), 251 (23), 219 (100), 187 (40), 161 (20) and 133 (48).

4.4.2. Dimethyl 1,1,3,5-tetramethyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-6,7-dicarboxylate-2,2-dioxide 3b. Compound **3b** was obtained as a white solid in 45% yield, mp 92.7–94.3 °C (from diethyl ether/hexane). IR (KBr) 1689, 1531, 1322, 1235, 1213, 1119 cm^{-1}. ^1H NMR 1.73 (3H, s), 1.76 (3H, s), 1.77 (3H, d, *J*=6.8), 2.43 (3H, s), 3.83 (3H, s), 3.84 (3H, s), 4.97 (1H, q, *J*=6.8). MS (EI) *m/z* 329 (M^+, 21%), 298 (20), 265 (23), 233 (64), 201 (39) and 147 (100). Anal. Calcd for $C_{14}H_{19}NO_6S$: C, 51.05; H, 5.81; N, 4.25. Found: C, 50.82; H, 5.70; N, 3.78.

4.4.3. 1,1-Dimethyl-3-benzyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-2,2-dioxide 3c. Compound **3c** was obtained as a white solid in 67% yield, mp 104.0–105.8 °C (from ethyl acetate/hexane). IR (KBr) 1712, 1704, 1323, 1219, 1114 cm^{-1}. ^1H NMR 1.66 (3H, s), 1.71 (3H, s), 1.97 (3H, s), 3.10 (1H, dd, *J*=6.4 and 15.0), 3.65 (1H, dd, *J*=6.4 and 15.0), 3.81 (3H, s), 3.84 (3H, s), 5.09 (1H, t, *J*=6.4), 7.13–7.34 (5H, m, Ar–H). ^{13}C NMR 11.6, 19.9, 25.8, 40.0, 52.1, 52.4, 62.2, 74.2, 112.8, 115.9, 128.5, 129.7, 130.1, 132.9, 134.2, 135.3, 164.8, 165.2. MS (EI) *m/z* 405 (M^+, 23%), 345 (38), 332 (68), 294 (100), 223 (49) and 173 (29). HRMS (EI) *m/z* 405.1255 ($C_{20}H_{23}NO_6S$ [M^+], 405.1246).

4.4.4. Dimethyl 1,1,5-trimethyl-3-phenyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-6,7-dicarboxylate-2,2-dioxide 3d. Compound **3d** was obtained as a white solid in 41% yield, mp 161.2–162.3 °C (from diethyl ether). IR (KBr) 1707, 1533, 1327, 1227, 1217, 1117 cm^{-1}. ^1H NMR 1.64 (3H, s), 1.79 (3H, s), 2.14 (3H, s), 3.85 (3H, s), 3.88 (3H, s), 5.94 (1H, s), 7.03–7.06 (2H, m, Ar–H), 7.44–7.46 (3H, m, Ar–H). ^{13}C NMR 11.5, 20.4, 25.2, 51.8, 52.0, 62.2, 76.2, 112.0, 115.7, 126.9, 129.4, 130.4, 130.5, 132.4, 135.7, 164.4, 164.7. MS (EI) *m/z* 391 (M^+, 13%), 360 (15), 327 (50), 275 (100), 263 (36) and 71 (82). Anal. Calcd for $C_{19}H_{21}NO_6S$: C, 58.30; H, 5.41; N, 3.58. Found: C, 58.65; H, 5.67; N, 3.26.

4.4.5. Dimethyl 1,3,5-trimethyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-6,7-dicarboxylate-2,2-dioxide 5. LiHMDS (2.4 mL, 1.0 M in hexanes, 2.4 mmol) was slowly added to a solution of dimethyl 3,5-methyl-1*H*,3*H*-pyrrolo[1,2-*c*][1,3]thiazole-6,7-dicarboxylate-2,2-dioxide **11** (0.5 g, 1.6 mol) in anhydrous THF (30 mL) at −78 °C and the mixture was stirred for 1 h. A solution of iodomethane (175 mL, 2.8 mmol, 1.7 equiv) was added slowly and the reaction mixture was stirred for 1 h. The reaction mixture was then allowed to warm to room temperature and quenched with saturated aqueous ammonium chloride solution (100 mL). The organic fractions were extracted with ethyl acetate (2×50 mL),

washed with water (50 mL), brine (50 mL) and dried over anhydrous $NaSO_4$. The solvent was removed in vacuo and the crude product was purified by flash chromatography (hexane/ethyl acetate) to give *dimethyl 1,3,5-trimethyl-1H,3H-pyrrolo[1,2-c]thiazole-6,7-dicarboxylate-2,2-dioxide* (0.414 g, 82%) as a white foam, together with 15% (0.076 g) of the starting material. IR (KBr) 1707, 1525, 1138 cm^{-1}. ^1H NMR 1.68 (3H, d, J=7.4), 1.74 (3H, d, J=7.1), 2.42 (3H, s), 3.83 (3H, s), 3.87 (3H, s), 4.58 (1H, q, J=7.4), 4.94 (1H, q, J=7.1). ^{13}C NMR 11.1, 17.6, 18.9, 51.6, 51.8, 57.2, 70.2, 111.4, 115.8, 131.9, 132.8, 163.1, 164.9. MS (EI) m/z 315 (M^+, 20%), 326 (30), 284 (15), 251 (39), 219 (74), 161 (27), 133 (100), 91 (11). HRMS (EI) m/z 315.0789 ($C_{13}H_{17}NO_6S$ [M^+], 315.0777).

4.5. General procedure for the sealed tube reactions

The appropriate 1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-6,7-dicarboxylate-2,2-dioxide (0.35 mmol) was dissolved in sulfolane (1 mL) in a glass pyrolysis tube, which was cooled in liquid nitrogen, evacuated, sealed and heated. After cooling to room temperature the tube was opened, the reaction mixture was diluted with dichloromethane and washed with water. The mixture was purified by flash chromatography [ethyl acetate/hexane (1:2) and then ethyl acetate/hexane (1:1)].

4.5.1. Dimethyl 2-isopropenyl-1,5-dimethyl-1*H*-pyrrole-3,4-dicarboxylate 7.[1b] Compound **7** was obtained from **3a** as a colourless solid in 40% yield, mp 68.0–69.4 °C (from ethyl acetate/hexane). ^1H NMR 2.02 (3H, br s), 2.42 (3H, s), 3.41 (3H, s), 3.78 (3H, s), 3.80 (3H, s), 5.03–5.04 (1H, m), 5.42–5.44 (1H, m).

4.5.2. Dimethyl 1-benzyl-2-isopropenyl-5-methyl-1*H*-pyrrole-3,4-dicarboxylate 15. Compound **15** was obtained from **3d** in 14% yield as an oil. IR (KBr) 1709, 1443, 1210 cm^{-1}. ^1H NMR 1.90 (3H, br s), 228 (3H, s), 3.80 (3H, s), 3.82 (3H, s), 4.98–4.99 (1H, m), 5.07 (2H, s), 5.32–5.34 (1H, m), 6.89–6.91 (2H, m, Ar–H), 7.25–7.34 (3H, m, Ar–H). ^{13}C NMR 11.2, 24.0, 47.5, 51.4, 51.6, 112.2, 113.0, 120.4, 125.5, 127.5, 128.9, 134.5, 135.7, 136.8, 137.7, 165.6, 165.8. MS (EI) m/z 327 (M^+, 35%), 295 (58), 263 (27), 259 (59) and 91 (100). HRMS (EI) m/z 327.1473 ($C_{19}H_{21}NO_4$ [M^+], 327.1471).

4.5.3. Dimethyl 1,2-dimethyl-5-vinyl-1*H*-pyrrole-3,4-dicarboxylate 19.[1b] Compound **19** was obtained from **17** as a colourless solid in 32% yield, mp 79.2–80.7 °C (from ethyl ether). ^1H NMR 2.45 (3H, s), 3.51 (3H, s), 3.80 (3H, s), 3.82 (3H, s), 5.42 (1H, dd, J=1.1 and 11.8), 5.54 (1H, dd, J=1.1 and 17.7), 6.66 (1H, dd, J=11.8 and 17.7).

4.6. General procedure for the flash vacuum pyrolysis

Pyrolysis of the appropriate 1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-2,2-dioxide (0.30–0.90 mmol) or vinyl-1*H*-pyrrole (0.20–0.35 mmol) at 700–850 °C/2×10^{-2}–5×10^{-2} mbar onto a surface cooled at −196 °C over a period of 1.5–5 h gave a yellowish pyrolysate (or red pyrolysate where indicated). (The rate of volatilization of the starting material was controlled by the use of a Kugelrohr oven, which heated the sample at 100–250 °C.) After cooling to room temperature the pyrolysate was removed from the cold finger with dichloromethane and the solvent was removed in vacuo.

4.6.1. Dimethyl 2-isopropenyl-1,5-dimethyl-1*H*-pyrrole-3,4-dicarboxylate 7 (70%)[1b] and 5-oxo-5*H*-pyrrolizine 8 (5%) from 3a [700 °C/2×10^{-2} mbar]. Product **7** was identified by comparison with the specimen previously prepared. *5-Oxo-5H-pyrrolizine* **8** was an oil with an intense orange colour. IR (KBr) 1740, 1711, 1241, 1124 cm^{-1}. ^1H NMR 2.04 (3H, s), 2.25 (3H, s), 2.26 (3H, s), 3.83 (3H, s), 5.50 (1H, s). ^{13}C NMR 9.8, 10.1, 16.2, 51.2, 115.8, 118.9, 121.4, 128.8, 138.2, 153.2, 164.4, 166.7. MS (EI) m/z 219 (M^+, 100%), 204 (17), 188 (17), 176 (38), 160 (24) and 148 (22). HRMS (EI) m/z 219.0894 ($C_{12}H_{13}NO_3$ [M^+], 219.0895).

4.6.2. 5-Oxo-5*H*-pyrrolizine 8 (15%) from 7 [850 °C/4×10^{-2} mbar]. Product **7** was identified by comparison with the specimen previously prepared.

4.6.3. Dimethyl 2-isopropenyl-1-ethyl-5-methyl-1*H*-pyrrole-3,4-dicarboxylate 10 (39%) from 3b [600 °C/2.0×10^{-2} mbar]. Product **10** was obtained as a yellow oil in 39% yield. ^1H NMR 1.24 (3H, t, J=7.2), 2.05 (3H, br s), 2.43 (3H, s), 3.78 (3H, s), 3.80 (3H, s), 3.84 (2H, q, J=7.2), 5.05 (1H, br s), 5.45 (1H, br s). ^{13}C NMR 10.9, 16.2, 24.2, 39.1, 51.3, 51.5, 111.8, 112.5, 120.3, 133.5, 136.0, 137.0, 165.7 and 165.8. MS (EI) m/z 265 (M^+, 40%), 233 (46), 218 (26), 201 (24), 173 (14) and 147 (100). HRMS (EI) m/z 265.1311 ($C_{14}H_{19}NO_4$ [M^+], 265.1314).

4.6.4. Methyl 1-ethyl-3,7-dimethyl-5-oxo-5*H*-pyrrolizine-2-carboxylate 11a and methyl 3-ethyl-1,7-dimethyl-5-oxo-5*H*-pyrrolizine-2-carboxylate 11b from 3b [750 °C/2.7×10^{-2} mbar]. Compounds **11a** and **11b** were obtained as a 54:46 mixture in 20% yield. IR (KBr) 1746, 1711, 1528, 1237, 1128 cm^{-1}. *Major component*: ^1H NMR 1.06 (3H, t, J=7.4), 2.25 (3H, s), 2.26 (3H, s), 2.51 (2H, q, J=7.4), 5.48–5.49 (1H, m). ^{13}C NMR 9.6, 15.3, 16.2, 17.6, 51.1, 115.1, 118.8, 128.1, 135.0, 138.2, 153.2, 164.2, 166.6. *Minor component*: ^1H NMR 1.15 (3H, t, J=7.4), 2.04 (3H, s), 2.25 (3H, s), 2.67 (2H, q, J=7.4), 5.48–5.49 (1H, m). ^{13}C NMR 9.9, 12.6, 16.2, 17.4, 51.1, 115.8, 119.0, 128.7, 132.2, 138.4, 153.2, 164.4, 166.3. MS (EI) m/z 233 (M^+, 72%), 218 (100), 202 (10) and 186 (12). HRMS (EI) m/z 233.1050 ($C_{13}H_{15}NO_3$ [M^+], 233.1052).

4.6.5. Methyl 1-ethyl-3,7-dimethyl-5-oxo-5*H*-pyrrolizine-2-carboxylate 11a and methyl 3-ethyl-1,7-dimethyl-5-oxo-5*H*-pyrrolizine-2-carboxylate 11b from 10 [750 °C/2.7×10^{-2} mbar]. Compounds **11a** and **11b** were obtained as a 62:38 mixture in 27% yield and were identified by comparison with the specimen previously prepared.

4.6.6. Dimethyl 1-phenylethyl-2-methyl-5-(1-isopropenyl-2-methyl)-1*H*-pyrrole-3,4-dicarboxylate 13 from 3c [650 °C/2.5×10^{-2} mbar]. Product **13** was obtained in 53% yield, mp 96 °C (from ethyl acetate/hexane). IR (KBr) 1721, 1705, 1227, 1330, 1123 cm^{-1}. ^1H NMR 2.02 (3H, d, J=0.9), 2.37 (3H, s), 2.87 (2H, approx. t, J=7.9), 3.78 (3H, s), 3.81 (3H, s), 3.99 (2H, approx. t, J=7.9),

5.03–5.04 (1H, m), 5.35–5.45 (1H, m), 7.05–7.33 (5H, m). ^{13}C NMR 11.0, 25.1, 37.4, 45.8, 51.4, 51.5, 111.8, 112.9, 120.5, 127.0, 128.6, 128.9, 133.8, 137.0, 137.6, 165.7 and 165.8. MS (EI) *m/z* 341 (M^+, 54%), 326 (30), 309 (49), 294 (100), 223 (53), 173 (42), 105 (40), 77 (19). HRMS (EI) *m/z* 341.1627 ($C_{20}H_{23}NO_4$ [M^+], 341.1627).

4.6.7. Dimethyl 1-benzyl-2-isopropenyl-5-methyl-1*H*-pyrrole-3,4-dicarboxylate 15 (33%) and dimethyl 2-methyl-5-(2-methyl-1-phenylallyl)-1*H*-pyrrole-3,4-dicarboxylate 16 (33%) from 3d [550 °C/2×10^{-2} mbar]. Product **15** was identified by comparison with the specimen previously prepared. *Dimethyl 2-methyl-5-(2-methyl-1-phenylallyl)-1H-pyrrole-3,4-dicarboxylate* **16**: IR (KBr) 1703, 1682, 1445, 1220, 1103 cm^{-1}. ^{1}H NMR 1.71 (3H, br s, H-9), 2.26 (3H, s, H-10), 3.68 (3H, s), 3.73 (3H, s), 4.45 (1H, br s, H-8a), 4.99 (1H, br s, H-8a), 5.20 (1H, br s, H-6), 7.10–7.12 (2H, m, Ar–H, *o*-H), 7.18–7.21 (1H, m, Ar–H, *p*-H), 7.25–7.28 (2H, m, Ar–H, *m*-H), 7.69 (1H, br s, NH). ^{13}C NMR 11.6 (C-10), 22.1 (C-9), 48.8 (C-6), 50.3 (CO_2CH_3), 50.4 (CO_2CH_3), 111.5 (C-3), 111.9 (C-4), 113.2 (C-8), 126.2 (*p*-C, Ar), 127.6 (*o*-C, Ar), 127.9 (*m*-C, Ar), 131.2 (C-7), 134.5 (*ipso*-C, Ar), 138.7 (C-2), 145.2 (C-5), 164.2 (CO), 164.7 (CO). MS (EI) *m/z* 327 (M^+, 8%), 295 (49), 263 (100), 235 (56) and 77 (4). HRMS (CI) *m/z* 327.1470 ($C_{19}H_{21}NO_4$ [M^+], 327.1471).

4.6.8. Dimethyl 2-methyl-5-(2-methyl-1-phenylallyl)-1*H*-pyrrole-3,4-dicarboxylate 16 from 15. Product **16** was obtained in 20% yield and was identified by comparison with the specimen previously prepared.

4.6.9. Dimethyl 1,2-dimethyl-5-vinyl-1*H*-pyrrole-3,4-dicarboxylate 19[1b] from 17 [700 °C/4×10^{-2} mbar]. Product **19** was obtained in 11% yield and was identified by comparison with the specimen previously prepared.

4.6.10. Methyl 1,3-dimethyl-5-oxo-5*H*-pyrrolizine-2-carboxylate 20 from 17 [850 °C/2.7×10^{-2} mbar]. Product **20** was obtained in 4% yield, mp 116.0–118.0 °C (from diethyl ether/hexane): IR (KBr) 1614, 1695 and 1729 cm^{-1}. ^{1}H NMR 2.11 (3H, s, H-8), 2.57 (3H, s, H-11), 3.73 (3H, s, H-10), 5.58 (1H, d, *J*=6.0, H-6), 7.12 (1H, d, *J*=6, H-7). ^{13}C NMR (off-resonance decoupling) 10.9 (q, *J*=129.2, C-8), 11.2 (q, *J*=130.7, C-11), 49.9 (q, *J*=147.4, C-10), 117.1 (s, C-2), 119.0 (d, *J*=181.9, C-6), 123.7 (s, C-1), 131.4 (s, C-7a), 135.9 (d, *J*=174.7, C-7), 141.3 (s, C-3), 164.3 (s, C-9), 165.6 (s, C-5). MS (EI) *m/z* 205 (M^+, 100%), 190 (24), 174 (69), 162 (16), 145 (45) and 117 (16). HRMS (CI) *m/z* 205.0746 ($C_{11}H_{11}NO_3$ [M^+], 205.0739).

4.6.11. Dimethyl 2-(but-3-en-2-yl)-5-methyl-1*H*-pyrrole-3,4-dicarboxylate 22, dimethyl 1-ethyl-2-methyl-5-vinyl-1*H*-pyrrole-3,4-dicarboxylate 23 and dimethyl 2-ethyl-5-methyl-1-vinyl-1*H*-pyrrole-3,4-dicarboxylate 24 from 5 [600 °C/2.5×10^{-2} mbar]. *Dimethyl 2-(but-3-en-2-yl)-5-methyl-1H-pyrrole-3,4-dicarboxylate* **22** was obtained as a colourless oil in 58% yield. IR (KBr) 1707, 1692, 1447, 1292, 1097 cm^{-1}. ^{1}H NMR 1.33 (3H, d, *J*=7.1), 2.38 (3H, s), 3.80 (3H, s), 3.81 (3H, s), 4.05–4.10 (1H, m), 5.12 (1H, approx. dt, *J*=7.7 and 1.4), 5.17 (1H, d, *J*=1.7), 5.93–6.04 (1H, m), 8.22 (1H, br s, NH). ^{13}C NMR 12.5, 18.6, 33.8, 51.3, 51.4, 111.7, 112.2, 115.1, 132.6, 138.0, 139.6, 165.7 and 165.8. MS (EI) *m/z* 251 (M^+, 12%), 220 (21), 204 (13), 187 (100), 177 (12), 159 (33), 132 (16), 118 (11). HRMS (EI) *m/z* 251.1164 ($C_{13}H_{17}NO_4$ [M^+], 251.1158).

Dimethyl 1-ethyl-2-methyl-5-vinyl-1H-pyrrole-3,4-dicarboxylate **23** was obtained in 5% yield. ^{1}H NMR 1.28 (3H, t, *J*=7.3), 2.47 (3H, s), 3.79 (3H, s), 3.83 (3H, s), 3.94 (2H, q, *J*=7.3), 5.38 (1H, dd, *J*=11.7 and 1.2), 5.58 (1H, dd, *J*=17.7 and 1.2), 6.59 (1H, dd, *J*=17.7 and 11.7). ^{13}C NMR 10.9, 15.5, 40.0, 51.3, 52.1, 111.4, 112.2, 118.6, 124.1, 130.3, 135.1, 165.7 and 165.8. MS (EI) *m/z* 251 (M^+, 35%), 220 (45), 190 (9), 161 (16), 133 (100), 118 (6). HRMS (EI) *m/z* 251.1146 ($C_{13}H_{17}NO_4$ [M^+], 251.1158).

Dimethyl 2-ethyl-5-methyl-1-vinyl-1H-pyrrole-3,4-dicarboxylate **24** was obtained in 14% yield. IR (KBr) 1708, 1443, 1214 cm^{-1}. ^{1}H NMR 1.14 (3H, t, *J*=7.5), 2.36 (3H, s), 2.79 (2H, q, *J*=7.5), 3.81 (6H, s), 5.32 (1H, d, *J*=15.7), 5.47 (1H, d, *J*=8.4), 6.63 (1H, dd, *J*=8.4 and 15.7). ^{13}C NMR 12.1, 14.0, 18.7, 51.4, 51.5, 111.9, 113.0, 115.8, 129.7, 133.2, 139.3, 165.8 and 166.0. MS (EI) *m/z* 251 (M^+, 42%), 236 (10), 219 (100), 204 (29), 187 (26), 161 (30), 133 (44), 118 (14). HRMS (EI) *m/z* 251.1161 ($C_{13}H_{17}NO_4$ [M^+], 251.1158).

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