Azafulvenium methides: new extended dipolar systems

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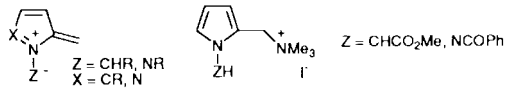
The transient 8π 1,7-dipolar azafulvenium methides 5 and 8 undergo sigmatropic [1,8] H shifts and the acyl derivatives 12 electrocyclise to give novel pyrrolooxazines 13; the related diazafulvenium methide 15 can be intercepted in 8π + 2π cycloadditions with silylated acetylenes.

1,3-Dipolar cycloaddition is an allowed 4π + 2π pericyclic process and has been of considerable value in organic synthesis.[1] 1,4-Sigmatropic shifts[2] and electrocyclic reactions[3] in 1,3-dipoles are also well established. However, although 1,5[4] and 1,7[5]-dipolar cyclisation are well recognised reactions, other pericyclic reactions of extended dipoles (those with more than 4π electrons) are less familiar.[6] In designing an extended dipole suitable for cycloaddition, competing electrocyclisation has to be prevented and the termini of the dipole must be a convenient distance apart for bonding to an appropriate cycloaddend. These principles are illustrated in the oxidopyridinium betaines, studied by Katritzky *et al.*,[6,7] which function as 4π 1,3-dipoles with 2π systems but as 6π 1,5-dipoles with dienes. We report here, our preliminary studies with the novel aza- and diaza-fulvenium ylide systems **1** (X = CR, N) which, in principle, can act as 4π 1,3-dipoles or as 8π 1,7-dipoles.

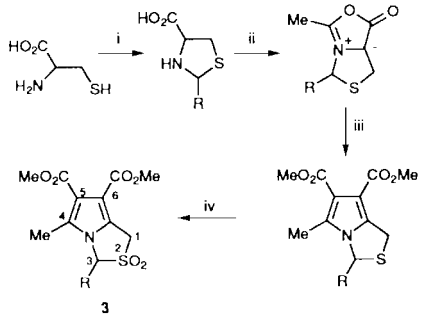
Initial, unsuccessful approaches towards the azafulvenium methides and imides **1** (X = CR) involved attempted base catalysed elimination from the pyrrole derivatives **2**. Earlier, an analogous elimination approach to systems of type **1** (X = CR)



1 **2**

by Padwa *et al.*[8] also failed. Padwa had also considered the thermal extrusion of SO_2 from the dihydrothienopyrrole *S,S*-dioxide **3** (R = H) but found it to be too thermally stable. Our own experience with extrusion of SO_2 from heterocyclic sulfones and with flash vacuum pyrolysis (FVP)[9] led us to reinvestigate this thermolysis. The sulfone **3** (R = H) did not extrude SO_2 when heated in solution at 300 °C. However, on FVP at 700 °C/10^{-3} mm SO_2 was eliminated although no identifiable products arising from the dipole were detected on the cold receiver. Intermolecular trapping was attempted by cocondensation 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 dimethyl acetylenedicarboxylate below −100 °C. No evidence was obtained for the formation of adducts.

Encouraged by the extrusion of SO_2 we designed derivatives for which the formation of the dipole might be revealed by intramolecular trapping in the FVP experiment. Introduction of aryl groups (phenyl, 4-anisyl and 2-thienyl) at the 3-position was accomplished using the appropriate aldehyde in the synthesis of the thienopyrrole (Scheme 1). However, on FVP, there was no evidence for electrocyclisation of the type seen with *ortho*-quinodimethanes.[9] On the other hand, introduction of methyl groups at both the 1- and the 3-positions led to vinylpyrroles **6** and **9**, respectively, on FVP. Their formation



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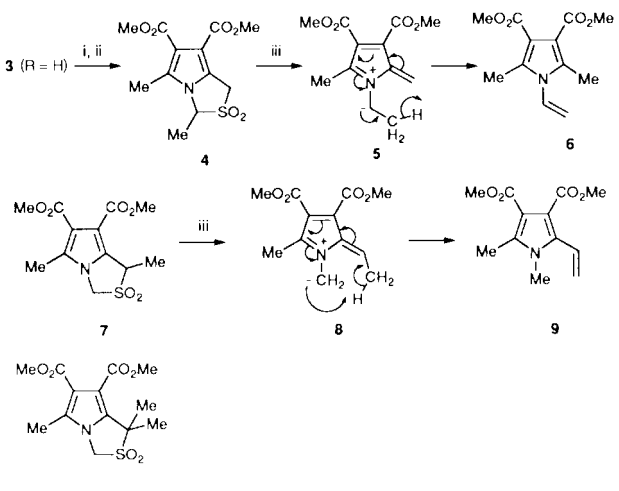
Scheme 1 *Reagents and conditions*: i, RCHO; ii, Ac_2O/heat; iii, DMAD; iv, MCPBA.

can be explained by allowed, suprafacial [1,8] H shifts in the 8π, 1,7-dipolar systems **5** and **8**, respectively. Synthesis of the 3-methyl derivative **4** was achieved by use of acetaldehyde in the route to the thienopyrrole (Scheme 1) and the 1-methyl derivative **7** was obtained from sulfone **3** (R = H) by methylation using LHMDS and iodomethane. Subsequent methylation of the 1-methyl compound **7** gave the 1,1-dimethyl derivative **10**. As expected the 1-proton in **3** (R = H) is more acidic than the 3-proton since it is activated by the 6-ester group.

The reaction of the 3-methyl derivative **4** to give the *N*-vinylpyrrole **6** was clean but the 1-methyl compound **7** gave the 2-vinylpyrrole **9** contaminated with an unidentified product showing vinylic H in the NMR spectrum. For sigmatropic shifts to occur the methyl groups must adopt an inward 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 is not unreasonable. The difference between the two derivatives **4** and **7** may reflect the differing ease with which the dipoles can attain the required configurations having inward methyl groups (only the inward configurations are illustrated in Scheme 2). Significantly, the reaction of



4 **5** **6** **7** **8** **9** **10**

Scheme 2 *Reagents and conditions*: i, LHMDS; ii, MeI; iii, 700 °C/10^{-3} mm.

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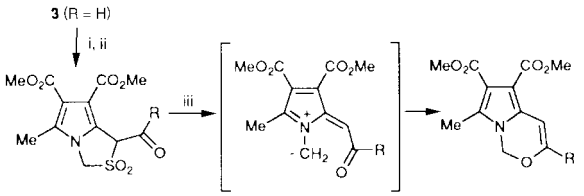
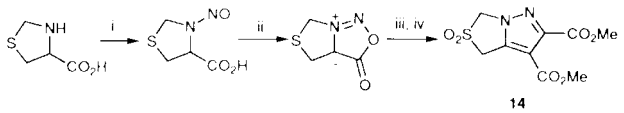


R	% yield 11	% yield 13
Me	40	52
MeO	38	–
Ph	69	86
4-MeC_6H_4	79	85
4-ClC_6H_4	40	76
3,4-$F_2C_6H_3$	51	60
2-furyl	64	72
cyclohexyl	88	68

Scheme 3 *Reagents and conditions*: i, LHMDS; ii, RCOCl; iii, 200 °C/1,2,4-trichlorobenzene.

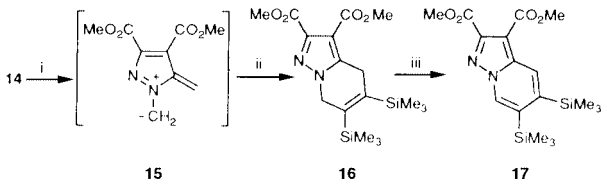
the 1,1-dimethyl derivative **10** where one of the methyl groups must necessarily be inward was cleanest.

A series of 1-acyl derivatives **11**† (Scheme 3) was also obtained by treatment of sulfone **3** (R = H) with LHMDS followed by an acyl chloride. Optimum conditions involved sequential treatment with base (1 equivalent), acyl chloride (1 equivalent) followed by further equivalents of base and acyl chloride. On FVP (600 °C/10^{-3} mm) the benzoyl derivative **11** (R = Ph) gave the pyrrolooxazine **13** (R = Ph), the first example of this new ring system and further strong evidence for generation of the desired dipolar system. Introduction of the acyl group lowers the temperature required for extrusion of SO_2 and the reaction, which can be carried out in solution at 200 °C, is general for all the acyl derivatives (Scheme 3).† The ability to generate the dipole in solution opened up the possibility of intermolecular trapping in a cycloaddition but extrusion of SO_2 in the presence of *N*-phenylmaleimide, dimethyl acetylenedicarboxylate or bis(trimethylsilyl)acetylene gave only the oxazine and no trace of cycloadduct. Prolonged heating of the oxazine in the presence of the dipolarophiles gave only recovered starting material and there was no evidence for reversibility in the electrocyclic ring closure.



Scheme 4 *Reagents and conditions*: i, $NaNO_2$/HCl; ii, TFAA/Et_2O; iii, DMAD; iv, MCPBA.

The pyrazole analogue **14** was obtained as shown (Scheme 4). Alkylation and acylation of **14** proved difficult but extrusion of SO_2 from this unsubstituted sulfone occurs more easily and can be achieved in solution. The extra pyrazole ring N thus appears to exert the same effect as an electron withdrawing acyl group at the 1-position of the pyrrole system. Extrusion of SO_2 in refuxing 1,2,4-trichlorobenzene in the presence of *N*-phenylmaleimide or dimethyl acetylenedicarboxylate gave no adducts but in the presence of bis(trimethylsilyl)acetylene (a reactive electron rich dienophile at high temperatures[10]) a cycloadduct **16** was obtained in 34% yield providing the first evidence for formation of these dipolar systems by intermolecular trapping (Scheme 5).† When the reaction was carried



Scheme 5 *Reagents and conditions*: i, 230–300 °C; ii, bis(trimethylsilyl)-acetylene; iii, prolonged heating.

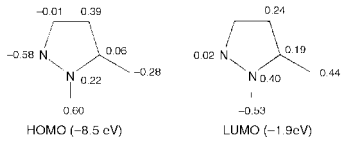


Fig. 1 MO coefficients of diazafulvenium methide.

out in a sealed tube with prolonged heating the aromatised adduct **17** was isolated (24%) (Scheme 5)†. Under similar conditions trimethylsilylacetylene gave a mixture of regioisomers. It may be significant that the dipolar systems undergo cycloaddition only with the electron rich dipolarophile and that addition occurs across the 1,7 and not the 1,3 positions. Molecular orbital calculations[11] for the pyrazole derivative (Fig. 1) indicate that dipole LUMO–dipolarophile HOMO interactions are dominant and that the MO coefficients are larger at the 1 and 7 positions than at the 3 position.

Notes and references

† *Selected data*: **11** (R = Ph): mp 221–222 °C, $\delta_H(CDCl_3)$ 2.47 (s, 3H, 5-Me), 3.58 and 3.86 (2 × s, 2 × 3H, ester Me), 4.99 (d, 1H, *J* 11 Hz, H-3) 5.07 (d, 1H, *J* 11 Hz, H-3′), 6.46 (s, 1H, H-1), 7.57–8.09 (m, 5H, aromatic H). **13** (R = Ph): oil, $\delta_H(CDCl_3)$ 2.41 (s, 3H, 7-Me), 3.85 and 3.86 (2 × s, 2 × 3H, ester Me), 5.66 (s, 2H, CH_2), 6.96 (s, 1H, CH), 7.33–7.71 (m, 5H, aromatic H). **16**: oil, $\delta_H(CDCl_3)$ 0.24 and 0.26 (2 × s, 2 × 9H, $SiMe_3$), 3.75 (t, 2H, *J* 5 Hz, CH_2), 3.82 and 3.92 (2 × s, 2 × 3H, ester Me) and 4.73 (t, 2H, *J* 5 Hz, CH_2). **17**: oil, $\delta_H(CDCl_3)$ 0.42 and 0.43 (2 × s, 2 × 9H, $SiMe_3$), 3.94 and 4.03 (2 × s, 2 × 3H, ester Me), 8.45 and 8.59 (2 × s, 2 × 1H, aromatic H).

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