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1-and 2-Azafulvenes

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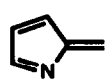
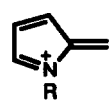
Abstract: **Flash pyrolysis of dialkylaminopyrroles and thermolysis of 2-pyrrylmethyl phenyl sulfoxide at 65°C in solution gave azafulvenes which were trapped with a variety of nucleophiles.**

1-Azafulvenes **1** and their salts **2** have been widely implicated as intermediates in pyrrole chemistry and a number of stabilised 6-substituted derivatives have been described.[1] However, the parent system has never been isolated, nor have simple derivatives been prepared in such a way that their chemistry, in particular cycloadditions, could be explored under controlled conditions. Flash pyrolytic elimination and condensation of the pyrolysate at low temperature offers the best possibility of achieving this objective and we report here our studies in this area. We also describe a simple, mild thermal route to **1** in solution.

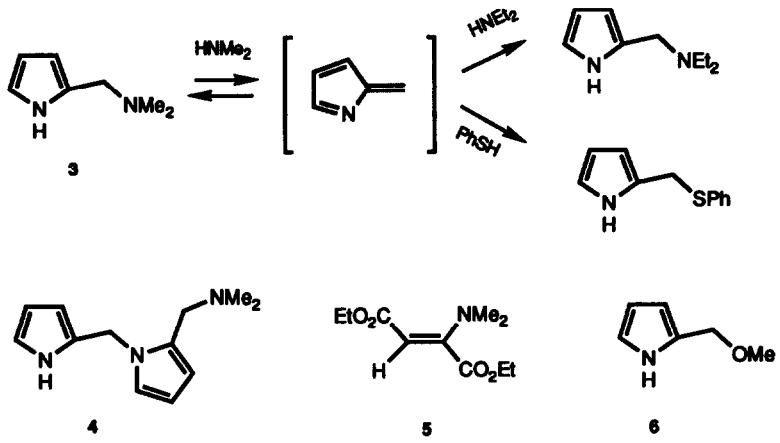


1

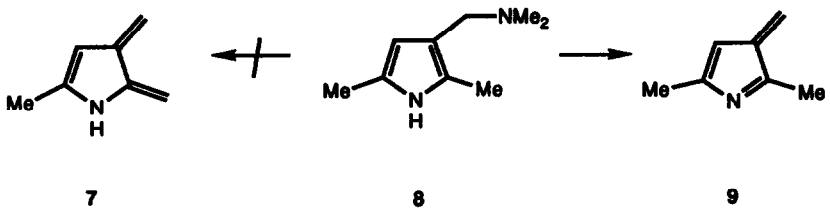


2

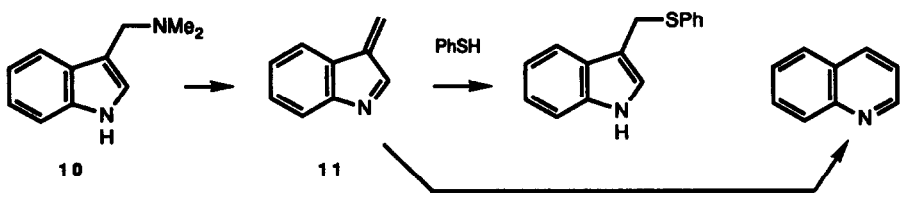
Flash pyrolysis of the readily available 2-dimethylaminomethylpyrrole **3** [2] (650°C/10^{-3}mmHg) and condensation of the pyrolysate on a cold surface at -196°C followed by warming to room temperature gave recovered **3** in virtually quantitative yield. However, co-condensation of the pyrolysate at -196°C with an excess of diethylamine gave 2-diethylaminomethylpyrrole on warming to room temperature revealing that elimination had occured to give **1** which undergoes nucleophilic attack at the electrophilic C-6 to regenerate the dialkylaminomethylpyrrole. Similar trapping was achieved by co-condensation with thiophenol but not with the less nucleophilic methanol or with acetic acid.[3] Condensation of the pyrolysate at -78°C in the absence of a trap gave the amine **4** (40%) together with **3** (40%); presumably at this higher temperature condensation of the dimethylamine is less effective and **3**, regenerated by addition of Me_2NH to **1**, also adds to **1**. Azafulvene **1** could act as a 2π, 4π or 6π system in cycloadditions. However, attempts to intercept **1** by co-condensation of the pyrolysate with cyclopentadiene and dimethyl acetylenedicarboxylate failed; in both cases readdition of dimethylamine to the azafulvene was predominant and in the case of DMAD the adduct of DMAD with dimethylamine **5** was also observed.[4] The azafulvene could not be detected directly as a stable entity even at low temperature but its appreciable lifetime was demonstrated by condensation in a dichloromethane matrix at -196°C. After 1h this was allowed to thaw (-96°C) and drip into a solution of diethylamine in dichloromethane at -78°C to give the diethylamine adduct in 50% yield together with regenerated starting material **3**.



In view of the failure of methanol to act as a nucleophilic trap for **1** the methoxy compound **6** [5] was considered as a precursor for which reattack by the leaving group would not compete so effectively with other traps. The methoxy compound underwent elimination at 950°C and the pyrolysate gave only polymer on warming to room temperature. Diethylamine as co-condensate was an effective trap but attempted cycloadditions with cyclopentadiene, 2,3-dimethylbutadiene and tetraphenylcyclopentadienone failed.

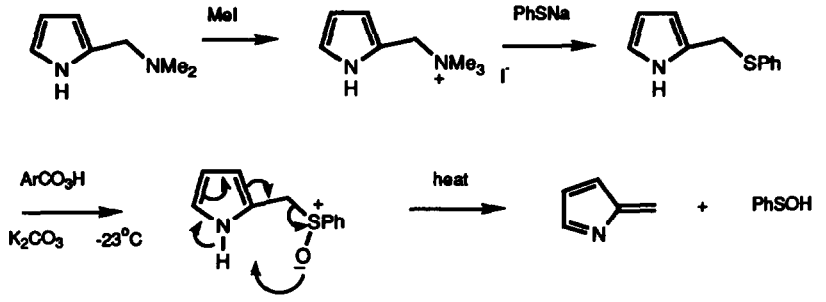


3-Dimethylaminomethyl-2,5-dimethylpyrrole **8** [6] on flash pyrolysis at 700°C gave the 2-azafulvene **9** which was again trapped with diethylamine and thiophenol but not with methanol or 2,3-dimethylbutadiene. In this case, concerted 1,4-elimination of the N-H and NMe_2 group is not possible and an alternative mechanism is 1,2-elimination preceded by two 1,5-shifts. Significantly, even when a large excess of diethylamine or thiophenol was present in the co-condensate an appreciable proportion of starting material **8** was detected. This possibly suggests that elimination for **8** is less facile than for **3**. There is no evidence for a 1,4-elimination of C-H and NMe_2 in **8** leading to the pyrrole xylylene **7** which, by analogy with other heterocyclic xylylenes,[7] might be expected to give two regioisomeric adducts with thiophenol and to be inert to diethylamine.

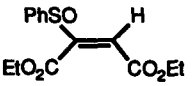


3-Dimethylaminomethylindole **10** gave the benzofused 2-azafulvene **11** on flash pyrolysis at 700°C as evidenced by trapping with thiophenol. Flash pyrolysis at a higher temperature (800°C) gave quinoline inter alia as reported by Brown.[8] Our trapping experiment therefore supports his suggestion that the 2-azafulvene may be an intermediate in this ring expansion. Pyridine was also formed from **3** at high pyrolysis temperatures especially when the pyrolyses were carried out over a SiO_2 catalyst.

Scheme



12



13

Attempts to intercept the azafulvene **1** produced by flash pyrolysis in cycloadditions failed either because of preferential reattack by nucleophilic leaving groups or polymerisation favoured by the high local concentration of the azafulvene. This makes a precursor which would undergo facile thermal elimination in solution to give a non-nucleophilic fragment highly desirable. Thermal 6-electron cycloelimination reactions of amine oxides, sulfoxides and selenoxides through a five membered transition state are well known and widely used analogues of the retro-ene reaction.[9] The sulfoxide **12** seemed worthy of investigation because a thermally allowed 10π cycloelimination through a six membered transition state appears feasible. The sulfoxide was obtained[10] in high yield as shown in the Scheme, the key to success being the low temperature sulfoxidation with *meta* chloroperbenzoic acid in the presence of solid K_2CO_3. At room temperature extensive decomposition occurred and with sodium or tetrabutylammonium periodates only low yields of sulfoxide were obtained together with intractable material.[11] The sulfoxide **12** undergoes thermal decomposition in solution (6 h at 65°C or 1 h at 110°C) and in the presence of diisopropylamine, sec-butylamine, thiophenol, ethanol, butanol and cyanide ion the expected adducts were formed in high yields.[12] Thus, when generated under these conditions, the azafulvene is more amenable to interception with a range of nucleophiles. In order to verify that these reactions involved an elimination-addition mechanism rather than S_N1 or S_N2 substitution of the sulfoxide moiety the N-methyl derivative of **12** (12, Me for H) was made by the same route. This compound, for which a concerted elimination is not possible, proved to be inert under the reaction conditions and was recovered unchanged from heating in toluene at 110°C for 12h. We believe this facile elimination of phenylsulfinic acid from **12** to be the first example of a 10π analogue of the retro-ene reaction. Attempts to intercept the azafulvene by heating sulfoxide **12** in toluene in the presence of cyclopentadiene, 2,3-dimethylbutadiene, tetraphenylcyclopenta-

dienone, 1-methoxy-3-trimethylsilyloxybutadiene, C-4-methoxyphenyl-N-phenylnitrone and diethyl acetylenedicarboxylate again failed to give any cycloadducts. In the case of DEAD the adduct **13** of the eliminated phenylsulfinic acid with DEAD was isolated giving further support to the elimination-addition sequence proposed for the formation of the azafulvene adducts in the presence of nucleophiles. In view of the ease of this 10π elimination it seemed possible that the azafulvene might also act as a 6π enophile in a reverse 10π ene reaction analogue. However, no adduct was observed with β-pinene.

In the 6-electron eliminations selenoxides are considerably more labile than the corresponding sulfoxides. The selenoxide **12** (Se for S) is extremely unstable but can be prepared *in situ* by oxidation of the selenide at -78°C, the latter being obtained as shown in the Scheme (Se for S). Oxidation of the selenide in the presence of diethylamine gave the expected adduct.

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REFERENCES AND NOTES

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2. Herz, W.; Dittmer, K.; Cristol, S.J. *J.Am. Chem. Soc.*, 1947, **69**, 1698.

3. Control experiments clearly establish that **3** did not react with diethylamine or thiophenol under more vigorous conditions than those involved in the reaction procedure.

4. Colourless oil: δ($CDCl_3$) 4.58 (1H, s, vinylic H), 3.96 (3H, s, OCH_3), 3.64 (3H, s, OCH_3), 2.88 6H, s, $N(CH_3)_2$); m/z 187.0847. $C_8H_{13}NO_4$ requires 187.0845.

5. Prepared (88%) from 2-dimethylaminomethylpyrrole by treatment with methyl iodide and then sodium methoxide in methanol. Colourless oil: δ ($CDCl_3$) 6.72 (1H, m, pyrrole 5-H), 6.14 (2H, m, 4-H, 3-H), 4.42 (2H, s, OCH_2), 3.31 (3H, s, OCH_3); $\nu_{max.}$ 3300 (NH) cm^{-1}; m/z 111.0683. C_6H_9NO requires 111.0684.

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9. Hoffmann, H.M.R. *Angew. Chem. Int. Ed.*, 1969, **8**, 556.

10. Colourless solid: m.p. 119.5°C., δ($CDCl_3$) 8.96 (1H, s, NH), 7.30 (5H, m, ArH), 6.67 (1H, m, pyrrole 5-H), 6.00 (1H, m, 3-H), 5.72 (1H, m, 4-H), 4.16 (1H, d, J = 14 Hz, CH_2SOPh), 3.98 (1H, d, J = 14 Hz, CH_2SOPh), $\nu_{max.}$ 3280 (NH), 1065 (SO) cm^{-1}.

11. A very recent paper describes the oxidation of a related pyrrole sulfide to a sulfoxide with sodium periodate. However, in that case the pyrrole was stabilised by an electron withdrawing group. Battersby, A.R.; Block, M.H.; Fookes, J.R.; Harrison, P.J.; Henderson, G.B.; Leeper, F.J. J. Chem. Soc. Perkin Trans., 1992, 2175.

12. Yields of unpurified adducts were greater than 90%. All new compounds had infrared and NMR spectra consistent with the proposed structures and gave satisfactory analytical and/or accurate mass spectral data.

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