COMMUNICATION

Pyrolytic cyclisation reactions of 3-azolylpropenyl alcohols; unexpectedly facile thermal decomposition of 5*H*-pyrrolo-[2,1-*a*]isoindole

Bernard A. J. Clark,[a] Xavier L. M. Despinoy,[b] Hamish McNab,*[b] Craig C. Sommerville[b] and Elizabeth Stevenson[b]

[a] *Kodak European Research and Development, Headstone Drive, Harrow, Middlesex, UK HA1 4TY*
[b] *Department of Chemistry, The University of Edinburgh, West Mains Road, Edinburgh, UK EH9 3JJ*

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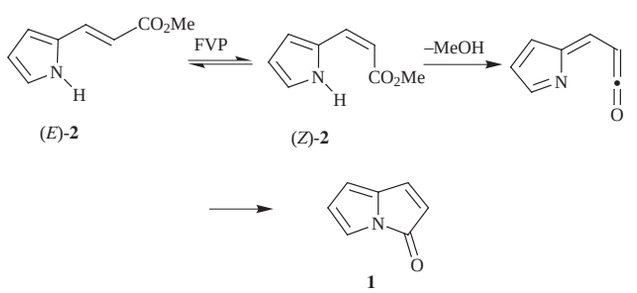
Flash vacuum pyrolysis (FVP) of 3-azolylpropenyl alcohols 5–7, 12 or 15 at 650–700 °C (10^{-2}–10^{-3} Torr) causes loss of water and cyclisation to give 3*H*-pyrrolizine 8 and its analogues 9, 10, 13 and 16; at higher temperatures (*e.g.* 900 °C) 5*H*-pyrrolo[2,1-*a*]isoindole 13 decomposes by loss of HCN to give naphthalene 18 and benzofulvene 19 and the mechanism of this transformation is studied by deuterium labelling.

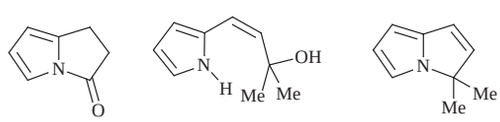
We have recently shown how pyrrolizin-3-one **1** and related heterocyclic systems can be efficiently prepared under flash vacuum pyrolysis (FVP) conditions by an elimination–electrocyclisation sequence from (*E*- or *Z*-) pyrroleprop-2-enoic esters **2** (*e.g.* Scheme 1).[1,2] If the *E*-ester is employed, a significantly higher furnace temperature must be used (up to 850 °C), but the excellent yields obtained even under such conditions are testimony to the remarkable thermal stability of the product lactams. We now report a modification of this chemistry which gives convenient syntheses of 3*H*-pyrrolizine and related ring systems by thermal cyclisation of (*Z*)-3-azolylpropenyl alcohols. In the course of this work we have also discovered a surprisingly facile thermal decomposition of 5*H*-pyrrolo-[2,1-*a*]isoindoles yielding benzofulvene and naphthalene and comment on the mechanism of this unexpected transformation.



(*E*)-**2** (*Z*)-**2** **1**

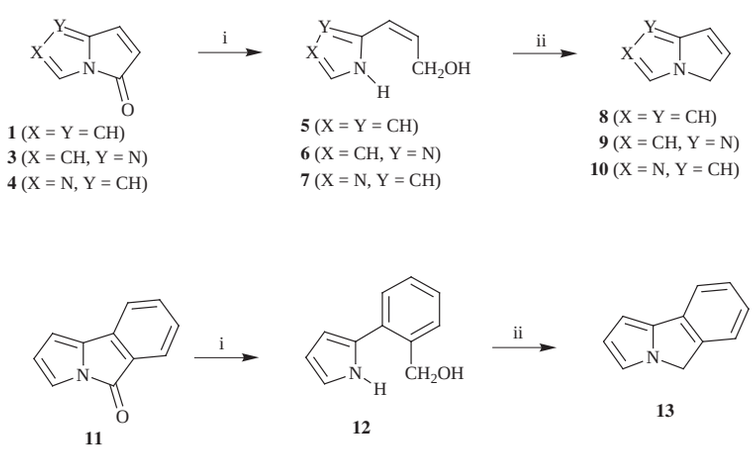
Scheme 1

The allylic alcohols **5**–**7** of the pyrrole and imidazole series were readily obtained (50–96%), exclusively in the *Z*-configuration, by lithium aluminium hydride reduction of the appropriate pyrrolizin-3-one **1** or azapyrrolizinone **3**, **4** in diethyl ether solution (Scheme 2). Similarly, the 2-arylpyrrole **12** was made by reduction of pyrrolo[2,1-*a*]isoindol-5-one **11**.[3] Other reducing agents show different regiochemistry; for example the softer reagent sodium borohydride reacts with pyrrolizin-3-one **1** in ethanol by conjugate addition to give the 1,2-dihydropyrrolizinone **14** as the predominant reduction product. 1,1-Disubstituted allylic alcohols can be obtained by reaction of pyrrolizin-3-one with organometallic reagents. For example the tertiary alcohol **15** was made in 96% yield from **1** and methyl lithium at −78 °C.



14 **15** **16**

Gas-phase pyrolysis of **5**–**7** (650 °C, 10^{-2}–10^{-3} Torr) and **12** (700 °C, 10^{-2} Torr) proceeded in analogous fashion to that of the ester **2**, *viz.* by elimination of water and electrocyclisation to give the products **8**–**10** and **13** respectively in 66–95% yield. These products are all known compounds and their spectra are in agreement with literature values.[4–6] At 650 °C, a number of



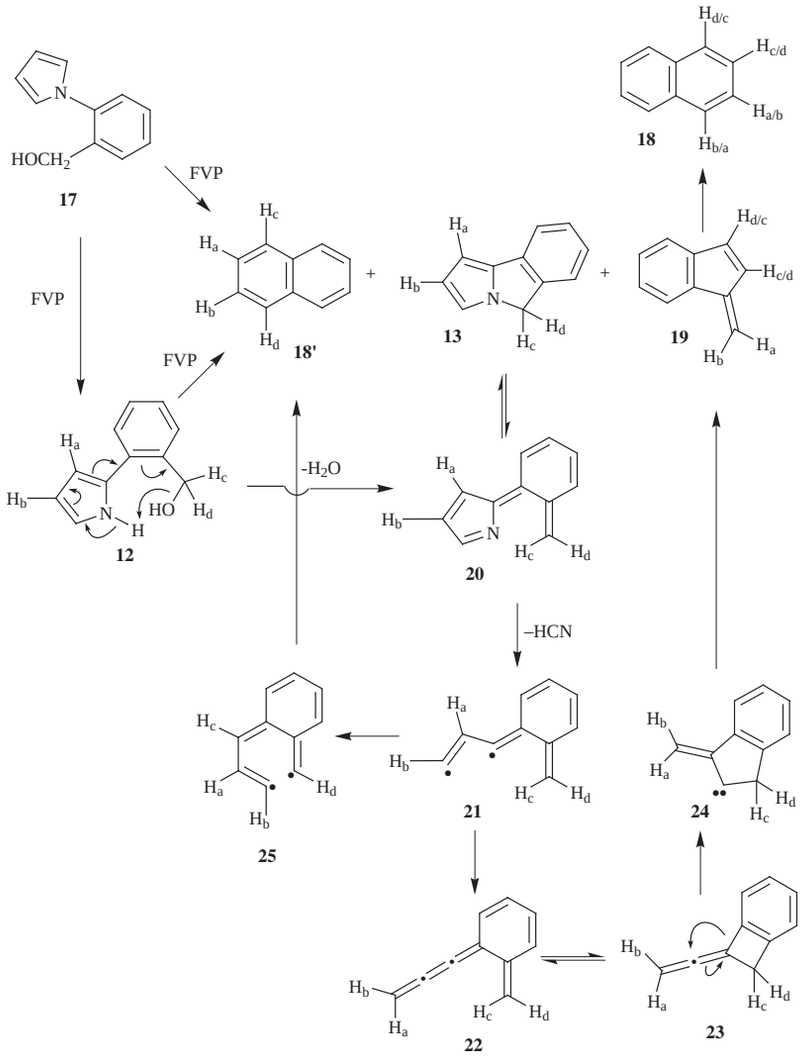
1 (X = Y = CH)
3 (X = CH, Y = N)
4 (X = N, Y = CH)

5 (X = Y = CH)
6 (X = CH, Y = N)
7 (X = N, Y = CH)

8 (X = Y = CH)
9 (X = CH, Y = N)
10 (X = N, Y = CH)

11 **12** **13**

Scheme 2 *Reagents and conditions*: i, $LiAlH_4$; ii, FVP.



Scheme 3

unidentified by-products were present in the pyrolysate from the tertiary alcohol **15**, but 3,3-dimethyl-3*H*-pyrrolizine **16**[7] was obtained in satisfactory yield and purity (64% after distillation) when the pyrolysis was carried out at 550 °C. This reductive ring-opening–pyrolysis sequence represents a general and convenient two stage deoxygenation of readily available pyrrolizin-3-ones and their analogues to the parent heterocyclic system. The final (electrocyclisation) stage is an aza-analogue of Griesbeck's route to dihydropentalenes.[8–10]

During the course of this work, we also studied the pyrolysis of the benzyl alcohol **17**[11] which we anticipated might lead to 5*H*-pyrrolo[2,1-*a*]isoindole **13** by a 1,5-aryl shift followed by elimination of water and electrocyclisation from **12** (*cf.* ref. 3). However, at furnace temperatures high enough to allow the initial rearrangement to proceed (900 °C, 10^{-2} Torr), the pyrroloisoindole was only a minor product and the major components of the pyrolysate were hydrocarbons derived from **13** by loss of HCN. A similar distribution of products was also obtained when **12** was pyrolysed at such temperatures, though the heterocycle **13** could be obtained in good yield by pyrolysis of **12** at 700 °C. The hydrocarbon products from the high temperature reactions were identified as naphthalene **18** and benzofulvene **19**[12] by comparison of their ^{1}H NMR spectra with literature data (Scheme 3).

The most likely mechanism for HCN loss from **13** involves initial ring-opening to the azafulvene valence isomer **20** followed by cleavage to give the key diradical intermediate **21**. The remaining steps of the mechanism were deduced from the results of a deuterium labelling study using **12** ($H_c = H_d = {}^2H$) as the precursor for the pyrolysis (900 °C, 10^{-2} Torr). ^{2}H NMR spectroscopy of the product mixture (Fig. 1) showed that the

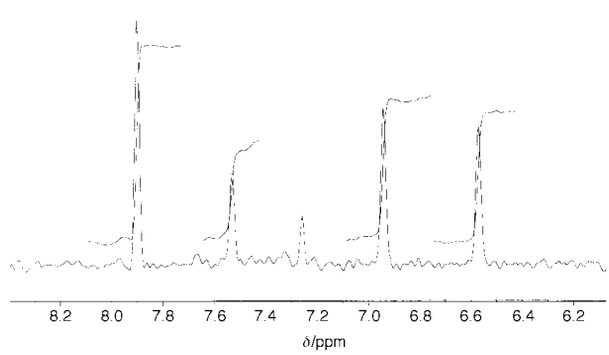


Fig. 1 ^{2}H NMR spectrum of the products obtained by FVP of **12** ($H_c = H_d = {}^2H$) at 900 °C (0.01 Torr); signals at δ 7.90 and 7.53 are due to naphthalene and those at 6.94 and 6.57 are due to benzofulvene. (The small peak at δ 7.25 is due to chloroform solvent.)

label resided at both the 1- and 2-position(s) of the naphthalene **18** and that two signals of equal intensity were found at positions corresponding to the ring alkene signals of the benzofulvene **19** ($H_c = H_d = {}^2H$); no label was found at other positions of **19**. The mechanism shown in Scheme 3 is consistent with these results. Thus, a 1,2-hydrogen atom shift of H_a in **21** gives the closed shell cumulene **22** which will exist in equilibrium with the benzocyclobutene **23**. The ring expansion to the carbene **24** (which is similar to a proposed stage in the mechanism of ring expansion of 3,4-bismethylenecyclobutene to fulvene[13]) leads to the benzofulvene **19** by subsequent insertion into the neighbouring CH_2 group. The known high temperature rearrangement of benzofulvene to naphthalene[14]

provides **18** with an equal amount of deuterium in the 1- and 2-positions, but it is clear that an additional route is required to account for the excess of label found in the 1-position (Fig. 1). It is likely that an alternative hydrogen shift in the diradical **21** leads to [1,4-$^2H_2$]naphthalene **18′** *via* the diradical **25**.

This mechanism of benzofulvene formation is similar to that recently suggested by Jones, Jr. and co-workers who proposed that the intermediates **22** and **23** were generated by isomerisation of benzocyclohex-1-en-3-yne at 640 °C.[15] Surprisingly, deuterium labels at H_a and H_b in the intermediates appeared at all alkene sites of the product **19** under their conditions and a skeletal rearrangement of **23** was proposed to explain these results.[15] Since we find that there is no such deuterium scrambling of our products generated at 900 °C, it follows (if our mechanism is correct) that the carbon skeleton of **23** and its isomers is stable at high temperatures and the rearrangement observed by Jones, Jr. and co-workers may therefore take place at an earlier stage of the mechanism. Further work is clearly required to resolve this anomaly.

Finally it is of interest to note the relative thermal lability of the pyrroloisoindole **13** by comparison with the corresponding lactams (*e.g.* **11**); possible reasons for this behaviour are under investigation.

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