Novel gas-phase cyclisation reactions of 2-(1-pyrazolyl)phenylnitrenes

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Flash vacuum pyrolysis of the azide 3 gives a mixture of pyrazolobenzotriazole 2, quinoxaline 5 and pyrazolobenzimidazole 4 derived from the corresponding nitrene.

In 1965 Lynch and Hung reported[1] that 1-(2-nitrenophenyl)pyrazole **1**, generated by deoxygenation of the corresponding nitro compound, cyclises in low yield to the pyrazolo[1,2-*a*]benzotriazole **2**. This work was optimised and extended in the 1970's by Meth-Cohn and co-workers[2,3] and more recently by Bettinetti's group[4,5] using solution thermolysis or photolysis of azides in addition to nitro compound deoxygenation as routes to the nitrene. They showed that the reaction is a singlet nitrene mediated process, and that electron withdrawing substituents in the benzene ring can increase the yield of mesomeric betaine product. The corresponding triplet nitrenes do not give useful cyclised products, but rather dimerise to azo-compounds or abstract hydrogen atoms from the solvent. Here, we report that our reinvestigation of this old reaction in the gas phase using flash vacuum pyrolysis (FVP) has revealed new and unexpected facets of this chemistry, including novel heterocyclisation processes not observed in the solution phase.

Sublimation of 1-(2-azidophenyl)pyrazole **3** at *ca.* 100 °C and 10^{-2} Torr into the silica furnace tube at 400–600 °C resulted in the formation of up to three products which could be separated by chromatography on silica. [CAUTION; azides are potentially explosive. Although we experienced no problems with these pyrolyses, carried out on a 0.2–4 mmole scale, all due precautions were taken–particularly the use of a metal inlet heater.] The products were identified as the pyrazolobenzo[1,2-*a*]triazole **2**, the pyrazolo[1,5-*a*]benzimidazole **4** and quinoxaline **5** by comparison of their spectra with literature values.[3,6] The distribution of these products at different furnace temperatures (Fig. 1) revealed an increase in the quinoxaline **5** level at high temperatures, apparently at the expense of the pyrazolobenzotriazole **2**. This was confirmed by repyrolysis of isolated pyrazolobenzotriazole **2**, which showed clean transformation to quinoxaline **5** with no trace of the pyrazolobenzimidazole **4** (Fig. 2). In contrast to the pyrazolo[1,2-*a*]benzotriazole case, pyrolysis of the azide **3** showed a relatively steady background of pyrazolobenzimidazole **4** which tailed off as the temperature was increased beyond 600 °C, yet pyrolysis of purified pyrazolobenzimidazole **4** at 700 °C demonstrated that it was stable, even at this temperature.

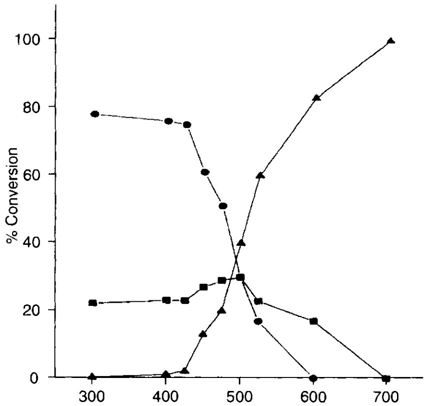


Fig. 1 Temperature dependence of the formation of **2** (●), **4** (■) and **5** (▲) by FVP of the azide **3**

We interpret these results as follows (Scheme 1). Pyrolysis of the azide at moderate furnace temperatures results in a mixture

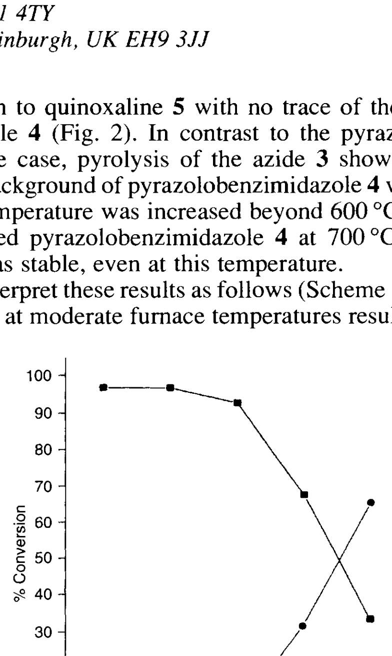
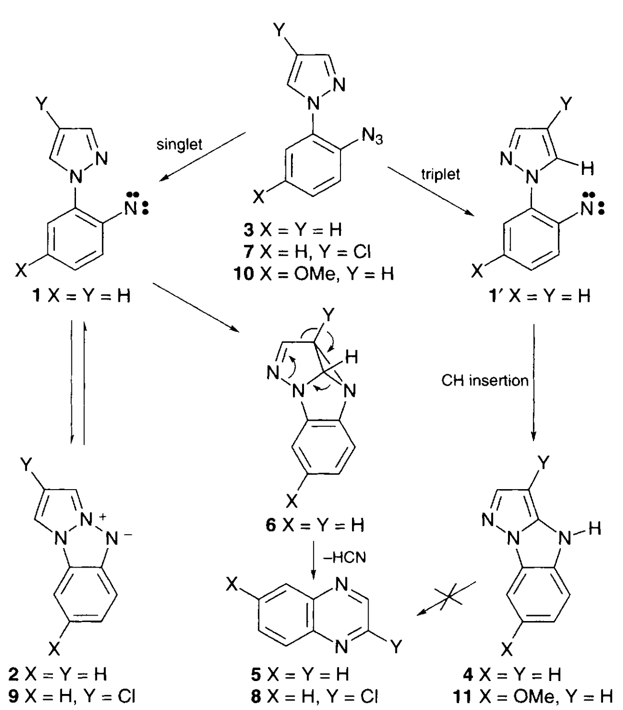


Fig. 2 Temperature dependence of the formation of **5** (●) by FVP of the betaine **2** (■)



Scheme 1

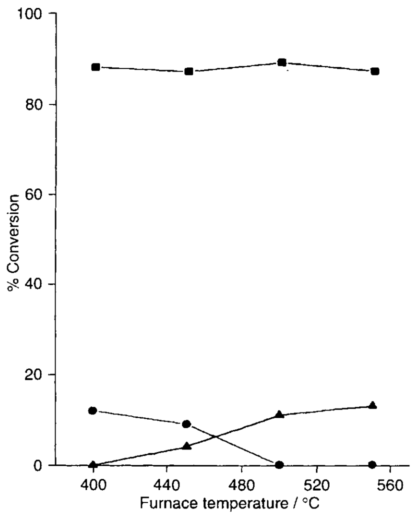


Fig. 3 Temperature dependence of the formation of **11** (■), **12** (●) and **13** (▲) by FVP of the azide **10**

of singlet and triplet nitrenes **1** and **1′** which, respectively, are trapped by the lone pair of the pyrazole 2-nitrogen atom to give **2**, and insert into the pyrazole 5-CH bond to give **4**. At 400 °C, the isolated yield of **2** (51%) is much improved over the best solution procedure (15%),[3] and the formation of **4** (21%) is the first example of 'useful' heterocyclic products being obtained *via* the triplet nitrene in these systems. Repyrolysis of the pyrazolobenzotriazole **2** does not regenerate the triplet nitrene and hence no further pyrazolobenzimidazole **4** is formed. Instead, a regenerated singlet nitrene can add to the 4,5 double bond of the pyrazole to give the heterosemibullvalene intermediate **6**, although an alternative concerted route from **2** to **6** cannot be excluded. The intermediate **6** can then collapse to quinoxaline **5** with loss of HCN, and this is the major process from **3** at high temperatures. This route is additionally favoured by the presence of a 4-chloro substituent on the pyrazole ring. Thus, at 450 °C, pyrolysis of the azide **7**† gave 54% of the quinoxaline **8** compound with 11% in the parent case, to the detriment of the yield of pyrazolo[1,2-*a*]benzotriazole **9**; this may be due to electron donation from the halogen increasing the electron density in the pyrazole system and hence favouring the nitrene addition mechanism.

Since it is most likely that **1** has a triplet ground state, it is possible that the absence of **4** from the pyrolysis of **3** at 700 °C—a temperature at which the pyrazolobenzimidazole is stable—may be due to an increased proportion of high energy singlet state being formed at these temperatures.

The earlier solution work[3] has indicated that the proportion of triplet-derived products may be increased by the presence of an electron donating substituent *para* to the incipient nitrene. We have confirmed this observation in spectacular fashion by FVP of the *p*-methoxy compound **10**, which shows almost exclusive formation of 7-methoxypyrazolo[1,5-*a*]benzimidazole **11** at all temperatures, with only a low background of 7-methoxypyrazolo[1,2-*a*]benzotriazole **12** and 6-methoxyquinoxaline **13** (Fig. 3). The pyrazolobenzimidazole **11** was isolated from a 500 °C pyrolysis in 92% yield after chromatography.

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Footnote

† All new compounds were characterised by their spectra and by elemental analysis or accurate mass measurement.

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