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Rearrangement and cyclisation reactions on the 1-arylpyrrol-2-iminyl – 2-aryliminopyrrol-1-yl radical energy surface

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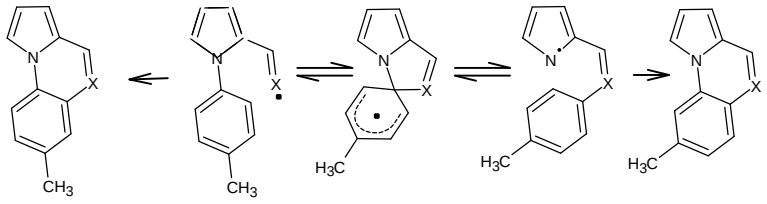
Abstract

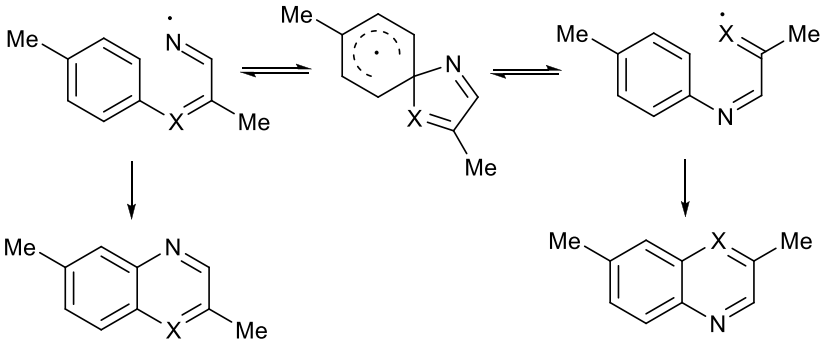
Independent generation of the iminyl (X = N) and pyrrol-1-yl (X = N) radicals by flash vacuum pyrolysis of the corresponding oxime ether and *N*-(dimethylamino) compound, respectively, provides two regioisomeric pyrrolo1,2-a]quinoxalines compounds. This shows that the radical species interconvert *via* the spirodienyl moeity at high temperatures. Corresponding generation of the pyrrol-1-yl (X = CH) radical gives the pyrrolo[1,2-*a*]quinoline as the only cyclised product. In this case, DFT calculations suggest that direct cyclisation of the pyrrol-1-yl takes place, rather than formation of the spirodienyl species and exclusive migration of the C-N bond.



Keywords: FVP, radicals, pyrroles, fused heterocycles

Introduction

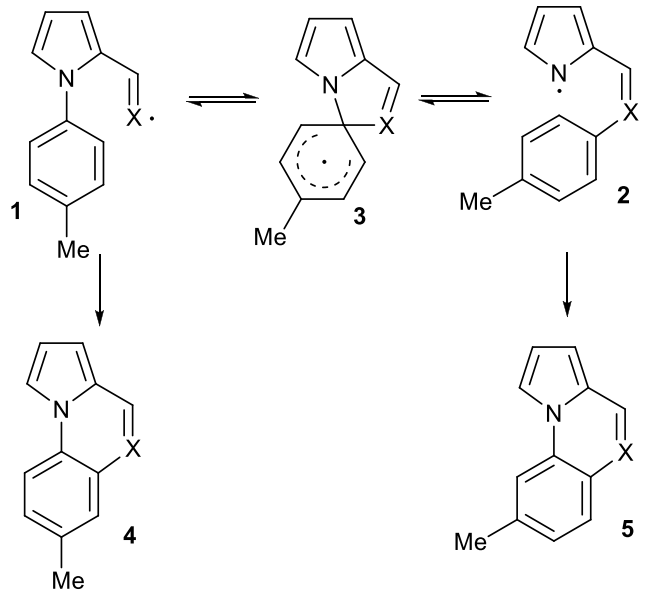
In previous papers we have explored the cyclisation reactions of iminyl radicals, generated in the gas-phase under flash vacuum pyrolysis (FVP) conditions.[1] In some cases, *e.g.* aryliminoiminyls, these reactions are dominated by *ipso*-attack and rearrangement *via* spirodienyl radicals (Scheme 1, X = N),[2] leading to mixtures of cyclisation products. The mechanism was supported by ^{15}N-labelling experiments.[3] However, corresponding rearrangements are not observed for arylvinyliminyls[4] (Scheme 1, X = CH), so the products must be formed either by direct cyclisation or by formation of the spirodienyl intermediate followed by exclusive migration of the C-N bond.



Scheme 1. Radical cyclizations forming quinoxalines.

The aims of the work reported here are summarised in Scheme 2. First, we hoped to generate the iminyl **1** (X = N) by the standard method involving FVP of the corresponding oxime ether. With two fused 5-membered rings, the spirodienyl intermediate **3** (X = N) is necessarily more strained than its analogue in Scheme 1 but, if rearrangement were to take place, generation of the pyrrol-1-yl radical **2** (X = N) would provide complementary entry to the energy surface. However, almost nothing is known about the synthetic organic chemistry of pyrrol-1-yl radicals except that a dimeric product is obtained when a vast excess of pyrrole is decomposed in the presence of *t*-butyl peroxide.[5] Tetraarylpyrrol-1-yl radicals have been characterised by EPR spectroscopy,[6] and more recently the pyrrol-1-yl radical itself has been implicated in UV photodissociation experiments[7] and its electron affinity has been measured.[8] Meanwhile, considerable theoretical work on the structure of the pyrrol-1-yl radical has been carried out.[8-13]

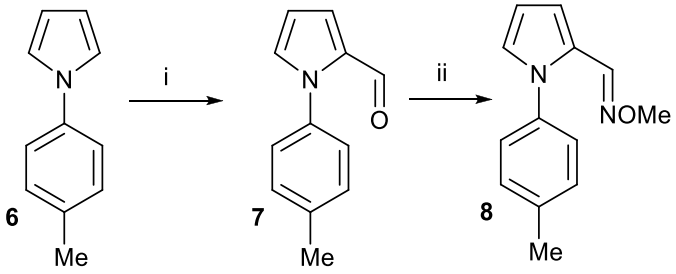
In the context of the present work, inventing a general FVP precursor to pyrrol-1-yl radicals for use in synthetic and mechanistic chemistry was therefore a major target. With a precursor for **2** (X = N) in place, the strategy was extended to the case of the 2-styrylpyrrolyl **2** (X = CH), though no attempt was made to create a route to the vinyl radical (**1**, X = CH). Finally, the mechanistic details of the rearrangement processes were analysed by DFT calculations at the B3LYP/cc-pVDZ level.



Scheme 2. Formation of pyrrolo[1,2-*a*]quinolines and quinoxalines.

Results and Discussion

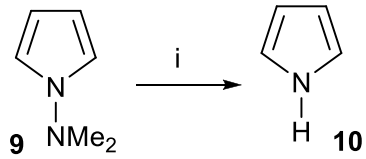
The iminyl precursor **8** was made by the route shown in Scheme 3. Vilsmeier formylation of 1-(*p*-tolyl)pyrrole **6** gave, in our hands, a mixture of the 2- and 3-formyl isomers, from which the 2-isomer **7** was obtained by recrystallisation (70%).[14] Condensation with *O*-methylhydroxylamine gave the oxime ether **8** (83%) as a mixture of *E*- and *Z*-isomers which were not separated.



Scheme 3. Preparation of the oxime ether **8.** *Reagents and conditions:* (i) DMF/$POCl_3$, 20 °C; (ii) $MeONH_2$ EtOH, reflux.

In order to design a precursor for the pyrrol-1-yl radicals **2**, it was essential for the molecule to have a weak N-Z bond which would cleave homolytically upon pyrolysis. Often we have used benzyl or allyl groups for this purpose,[1] but it is known that *N*-benzyl- or *N*-allyl- pyrrole undergoes rearrangement by 1,5-sigmatropic shifts rather than radical cleavage.[15] However, we have also shown that hydrazones are useful generators of iminyl radicals,[1,2] and so the possibility of using derivatives of *N*-(dimethylamino)pyrrole **9** was investigated. FVP of *N*-(dimethylamino)pyrrole **9** itself showed the formation of pyrrole **10**, as well as some unidentified products, which suggests that homolysis could be followed by hydrogen atom capture, a standard reaction of

aminyl and phenoxyl radicals (Scheme 4).[1] The temperature profile of the **9**→**10** conversion (Figure 1) shows that temperatures of 800-850 °C are required to complete the homolysis.



Scheme 4. Pyrolysis of 1-(dimethylamino)pyrrole. *Reagents and conditions:* (i) FVP, 850 °C.

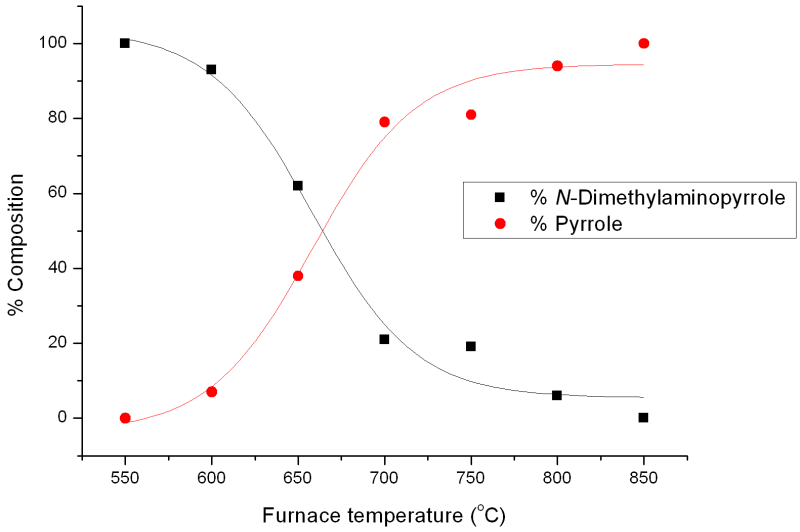
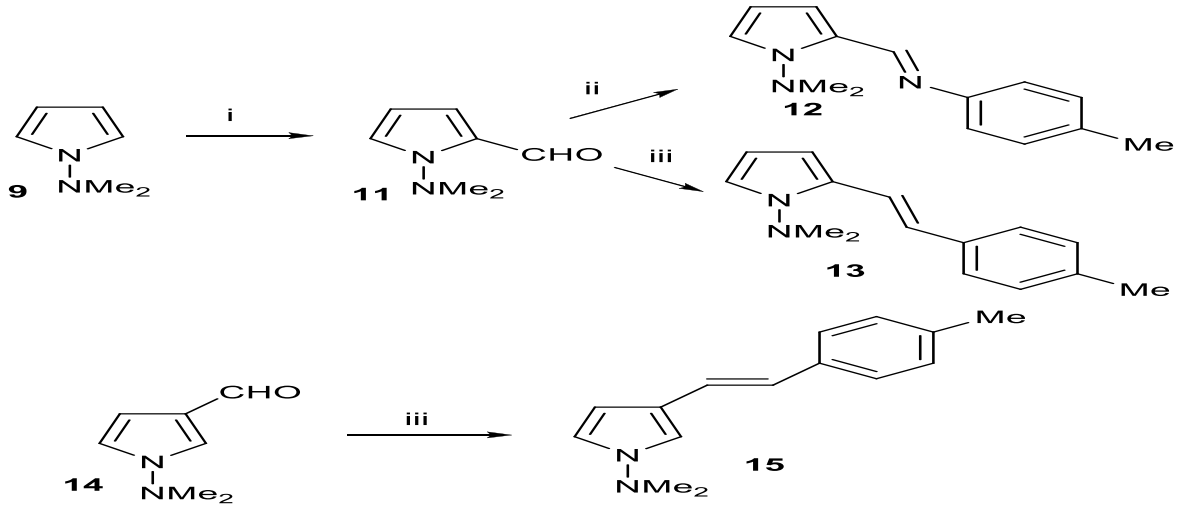
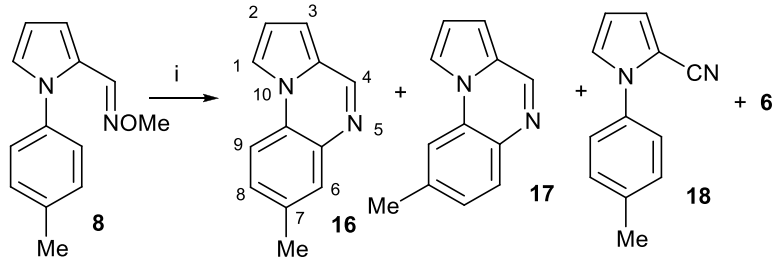


Figure 1. Temperature profile of **9**→**10** conversion.

Accordingly, a precursor to **2** (X = N) was made, in two steps. First, formylation of **9** was carried out by the literature method;[16] the 2-formyl isomer **11** was isolated as the major product (52%) after chromatography, though some of the 3-formyl product **14** was also obtained (12%). The imine **12** (97%) was synthesised by condensation with *p*-toluidine (Scheme 5). The precursor to **2** (X = CH) was made by Wittig reaction[16] of the aldehyde **11** with the corresponding ylide which gave the 2-styryl compound **13** (Scheme 5). The corresponding 3-styryl compound **15** was made similarly by reaction of the 3-formylpyrrole **14**. Only the trans isomers were detected in solution by nmr (^{3}J, 16Hz) FVP of the oxime ether **8** gave two heterocyclic products in essentially equal amounts (40% and 41% isolated yields), together with small amounts of 1-*p*-tolylpyrrole-2-carbonitrile **18** (8%) and 1-*p*-tolylpyrrole **6** (5%), all of which were separated by chromatography (Scheme 6). The heterocyclic products were identified as 7-methylpyrrolo[1,2-*a*]quinoxaline **16** and 8-methylpyrrolo[1,2-*a*]quinoxaline **17** by the NOESY data shown in Figure 2. Compound **16** is characterised by the correlation of a pyrrole proton at δ_H 7.86 (corresponding to H-1) with a doublet benzenoid proton at δ_H 7.82 (corresponding to H-9). Compound **17** is characterised by the correlation of a pyrrole proton at δ_H 7.91 (due to H-1) with a 'singlet' benzenoid proton at δ_H 7.68 (due to H-9).



Scheme 5. Preparation of the imine **12** and the styrylpyrroles **13** and **15.** *Reagents and conditions:* (i) DMF/$POCl_3$, 1,2-dichloroethane, reflux; (ii) *p*-$MeC_6H_4NH_2$, EtOH, reflux; (iii) Ph_3P=CHAr, toluene, reflux.



Scheme 6. Products of FVP of the oxime ether **8.** *Reagents and conditions:* (i) FVP, 650 °C.

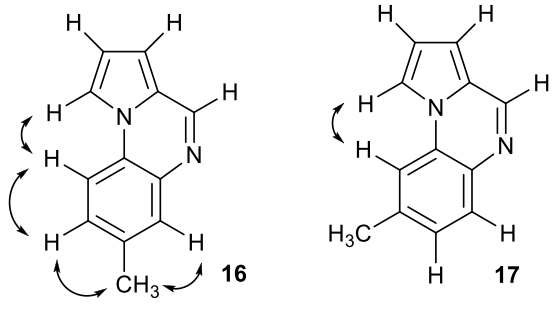
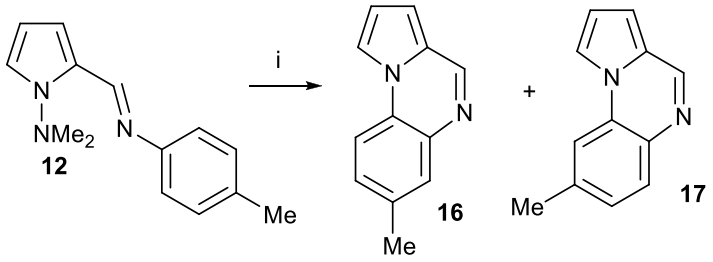


Figure 2. NOE data for **16** and **17**.

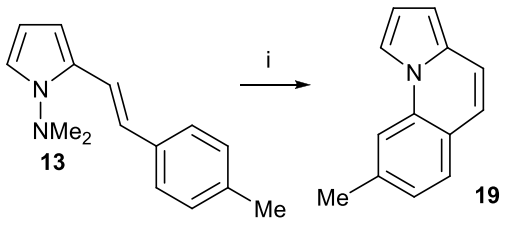
The formation and unambiguous characterisation of **16** and **17** suggests that the iminyl **1** (X = N) is able to undergo *ipso*-attack to generate the spirodienyl radical **3** (X = N) (Scheme 2) which subsequently rearranges to the two regioisomeric products. However, it is unclear whether interconversion *via* the spirodienyl is complete or whether this reaction mode competes with direct cyclisation at the *ortho*-position.



Scheme 7. Products of FVP of the dimethylaminopyrrole **12.** *Reagents and conditions:* (i) FVP, 800 °C.

More information on this point was gained by FVP of the *N*-dimethylaminopyrrole **12** at 800 °C (Scheme 7) which provided the two methylpyrrolo[1,2-*a*]quinoxalines **16** (23% of the mixture) and **17** (73% of the mixture) (4% of mixture not assigned). First, this provides further evidence that the pyrrol-1-yl radical **2** (X = N) can be generated by this route and that it is capable of cyclisation reactions to provide 6-membered ring products. Second, the formation of the two heterocyclic products **16** and **17** shows that at least some cyclisation *via* the spirodienyl must take place. However, the fact that these products were obtained in unequal ratio (in contrast to the result from FVP of **8**) is evidence that direct cyclisation must also play a part in the energy surface summarised by Scheme 2 (see later discussion) and provides the major product from the pyrrol-1-yl.

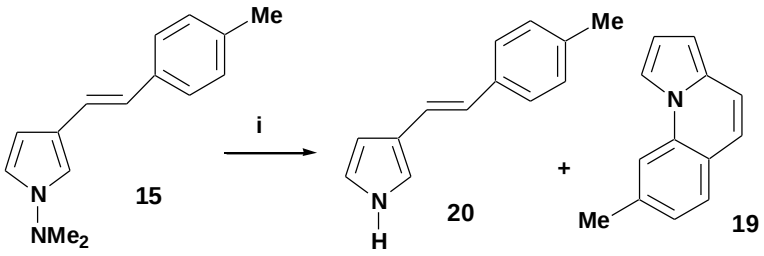
In contrast, FVP of the styryl compound **13** at 750 °C gave only 8-methylpyrrolo[1,2-*a*]quinoline **19** (50% yield) (Scheme 8). NOESY analysis confirmed the structure by correlation of a pyrrole proton with a 'singlet' benzenoid proton (*c.f.* **17** in Figure 2). In this case *E/Z*-isomerisation of the alkene **17** is followed by direct cyclisation at the *ortho*-position, or by spirodienyl formation followed by exclusive migration of the C-N bond. Such high regioselectivity has major advantages in the use of pyrrol-1-yl radicals as a synthetic route to unusual pyrrolo[1,2-*a*]quinolines.



Scheme 8. FVP of the 2-styryl pyrrole **13.** *Reagents and conditions:* (i) FVP, 750 °C.

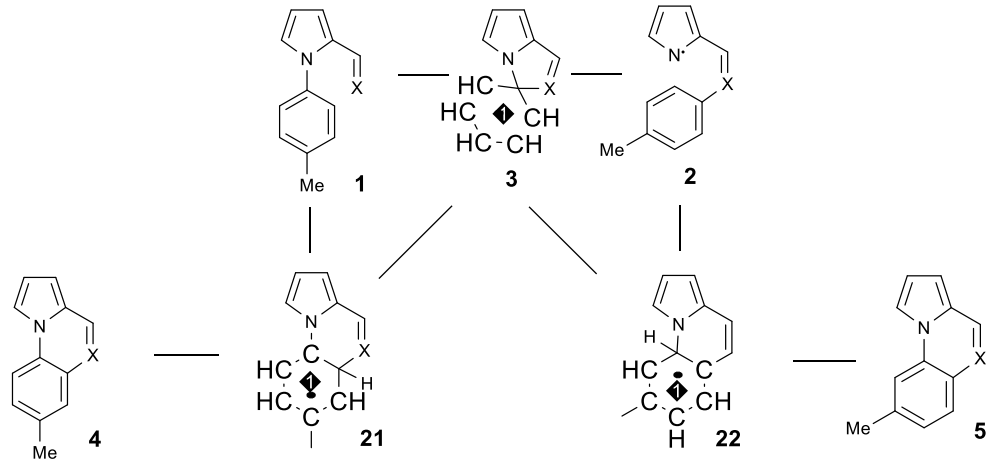
Only low yields of products could be isolated from FVP of the 3-styryl isomer **15** at 750 °C, which suggests that the 3-substituted pyrrol-1-yl radical has no clear route to products (Scheme 9). The two compounds that were isolated in greatest amounts were the known[18] deaminated pyrrole **20** (11%) (*c.f.* Scheme 4) a product of hydrogen-capture by the pyrrol-1-yl radical and 8-methylpyrrolo[1,2-*a*]quinoline **19** (5%). The formation of 8-methylpyrrolo[1,2-*a*]quinoline **19** requires rearrangement of the vinyl group from the 3-position to the 2-position of the pyrrole, followed by cyclisation. Such 1,5-shifts are well-known in the thermal chemistry of pyrroles,[15] and although the rearrangement is not normally quantitative at temperatures as low as 750 °C in our apparatus, they may well account for the formation of such a minor product (5%).

8-Methylbenzo[*g*]indole was tentatively identified in trace amounts from an impure fraction, and is consistent with delocalisation of the pyrrol-1-yl radical to the 2-position, followed by cyclisation. Clearly this is not a favorable process for the initial radical.



Scheme 9. FVP of the 3-styryl pyrrole **15.** *Reagents and conditions:* (i) FVP, 750 °C.

To summarise the experimental results: independent generation of the iminyl **1** (X = N) and of the pyrrol-1-yl **2** (X = N) radicals results in isomeric mixtures of the cyclisation products 7-methylpyrrolo[1,2-*a*]quinoxaline **16** (*i.e.* **4**, X = N) and 8-methylpyrrolo[1,2-*a*]quinoxaline **17** (*i.e.* **5**, X = N), though in different ratios from the two precursors. In contrast, generation of the pyrrol-1-yl **2** (X = CH) provides only 8-methylpyrrolo[1,2-*a*]quinoline **19** (*i.e.* **5**, X = CH). The situation is summarised in Scheme 10, an extension of Scheme 2, in which the iminyl **1** (X = N) is potentially in equilibrium with the direct cyclisation intermediate **21** (X = N) and the spirodienyl radical **3** (X = N). Similarly, the pyrrol-1-yl **2** (X = N) can equilibrate with its direct cyclisation intermediate **22** (X = N) and with the spirodienyl **3** (X = N).



Scheme 10. Radical pathways resulting in equilibration and isomeric products.

The energy surface of the *N*-phenyliminyl corresponding to **1** (X = N) was modelled by DFT calculations (B3LYP/cc-pVDZ) (Figure 3).[19] These show that the difference in barrier between the iminyl **1** (X = N) and the direct cyclisation intermediate **21** (X = N) and between the iminyl and the spirodienyl **3** (X = N) is 21.5 kJ mol^{-1} in favour of the direct cyclisation. The corresponding difference between the pyrrol-1-yl **2** (X = N), its direct cyclisation intermediate **22** (X = N) and the spirodienyl **3** (X = N) is 26.6 kJ mol^{-1}, again in favour of the direct cyclisation. This suggests that the direct cyclisation is relatively favoured kinetically in the case of the pyrrol-1-yl, as found by experiment. Thermodynamically, the spirodienyl **3** (X = N) lies 40.6 kJ mol^{-1} above the direct cyclisation intermediate **21** [from the iminyl **1** (X = N)] and some 59.9 kJ mol^{-1} above the direct cyclisation intermediate **22** [from the pyrrol-1-yl **2** (X = N)]. Again, direct cyclisation from the pyrrol-1-yl is relatively favoured thermodynamically, though it is somewhat surprising that the spirodienyl route can compete at all, given the high relative energies of its intermediate and transition states.

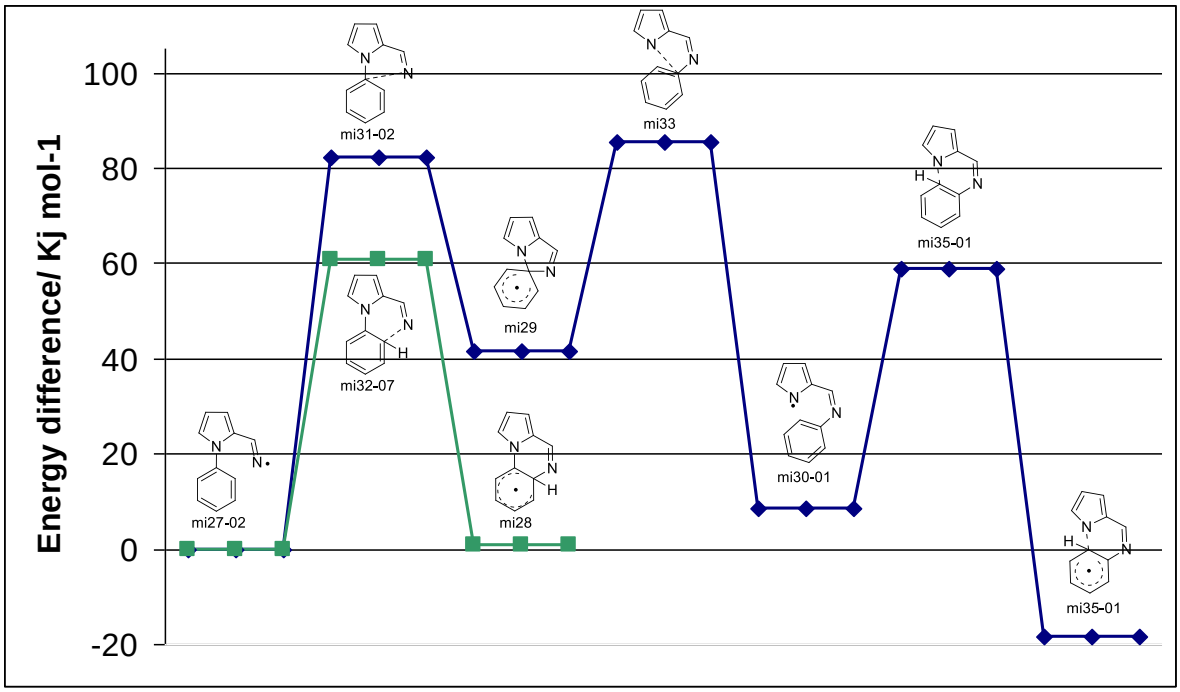


Figure 3. The iminyl **1** (X = N) – pyrrol-1-yl **2** (X = N) energy surface; codes refer to the structures given in the supplementary information.

By comparison, the difference in energy between the transition states relating the pyrrol-1-yl **2** (X = CH), its direct cyclisation intermediate **22** (X = CH) and the spirodienyl **3** (X = CH) is 55.6 kJ mol^{-1}, in favour of the direct cyclisation. Similarly, the energy of the spirodienyl **3** (X = CH) itself is some 72.9 kJ mol^{-1} higher than that of the direct cyclisation intermediate **21** (X = CH). The results of the calculations clearly suggest that only one isomer is formed by FVP of **12**, because direct cyclisation of the pyrrol-1-yl takes place, rather than formation of the spirodienyl and exclusive migration of the C-N bond. Nevertheless, cleavage of the C-N bond in the spirodienyl **3** (X = CH), if formed, is indeed favoured over C-C cleavage by 31.8 kJ mol^{-1}. The very high energy of the vinyl radical **1** (X = CH) may help to explain why no precursor of such species under FVP conditions is known.

Finally, it is worth noting that pyrrol-1-yl radicals generated by homolysis of the N-N bond, are formed as σ-radicals[20] (*e.g.* σ **23**) but intersystem crossing to the π-surface to give π-**23** is likely to be facile.[6] In practice the calculations show rather different electron density on the nitrogen in the 2 cases suggesting different character. Delocalisation of the π-radical might promote some reactivity at the 3-position of species such as **2**. In practice, whatever the electronic nature of the radical species involved, there is no doubt from the experimental results [including the very low yield of cyclisation product(s) by FVP of the 3-substituted precursor **15**] that the pyrrolyl radical species *behave* as σ- radicals localised on the nitrogen atom.

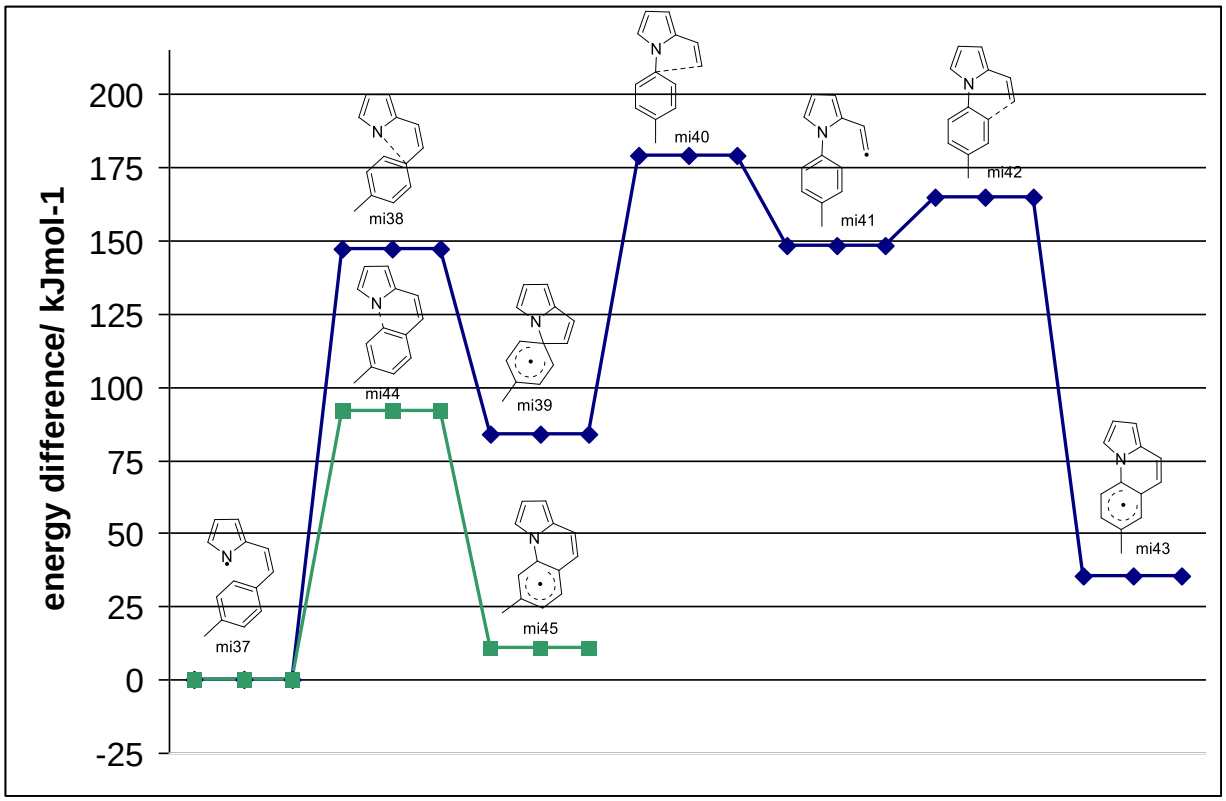


Figure 4. The vinyl **1** (X = CH) – pyrrol-1-yl **2** (X = CH) energy surface; codes refer to the structures given in the supplementary information.

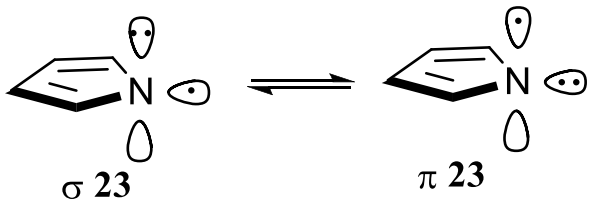


Figure 5. Representation of the σ and π pyrrol-1-yl radicals.

Conclusions

We conclude that FVP reactions of 1-aminopyrrole derivatives provide useful routes to pyrrol-1-yl radicals, whose cyclisation chemistry is explored here for the first time. Cyclisation of 2-vinylpyrrol-1-yls proceeds regiospecifically to provide an unusual route to the pyrrolo[1,2-*a*]quinoline ring system. On the other hand, cyclisation of pyrrol-1-yls containing an arylimino side chain takes place *via* spirodienyl radical formation and rearrangement, in competition with direct cyclisation. This result was confirmed by the cyclisation behaviour generation of an isomeric iminyl radical. Further reactions of azol-1-yl radicals will be reported in a subsequent paper.

Experimental Section

General. ^{1}H and ^{13}C NMR spectra were recorded at 200 (or 250) and 50 (or 63) MHz respectively for solutions in [^{2}H]chloroform unless otherwise stated. Coupling constants are quoted in Hz. Mass spectra were recorded under electron impact conditions.

1-(*p*-Tolyl)pyrrole 6. A mixture of *p*-toluidine (4.53 g, 42.3 mmol), 2,5-dimethoxytetrahydrofuran (6.01 g, 45 mmol) and glacial acetic acid (20 cm^3) was heated under reflux for 2 h. The volatiles were removed under reduced pressure, water (100 cm^3) was added and the reaction mixture extracted with dichloromethane (3 × 80 cm^3). The combined organic extracts were washed with water (80 cm^3), dried ($MgSO_4$) and concentrated to give crude **6** (5.71 g, 86%), mp 77-78 °C (lit.[21] 81-82 °C) δ_H 7.30-7.19 (4H, m), 7.06 (2H, t, ^3J 2.2), 6.33 (2H, t, ^3J 2.2) and 2.37 (3H, s); δ_C 138.3 (quat), 135.2 (quat), 129.9, 120.4, 119.2, 109.9 and 20.7; *m/z* 157 (M^+, 100%), 115 (39) and 91 (30).

1-(*p*-Tolyl)pyrrole-2-carbaldehyde 7. A solution of 1-*p*-tolylpyrrole **6** (4.023 g, 25.6 mmol) in DMF (40 cm^3) was added to a solution of phosphoryl chloride (5.19 g, 33.2 mmol) in DMF (85 cm^3) and stirred for 1 h. A further portion of phosphoryl chloride (5.19 g, 33.2 mmol) in DMF (85 cm^3) was added and stirring continued for another hour. The reaction mixture was poured onto crushed ice, hydrolysed with dilute aqueous sodium hydroxide (2 M, 200 cm^3) and acidified to pH 6-7 with dilute hydrochloric acid (2 M, 20 cm^3). The mixture was then extracted with ether (3 × 250 cm^3) and the combined organic extracts were washed with water (200 cm^3) and dried ($MgSO_4$). The solvent was removed under reduced pressure to give crude aldehyde as an orange oil. Distillation removed remaining traces of DMF and the aldehyde crystallised as an orange solid. TLC showed that formylation had occurred at both the 2- and 3-positions and so the mixture was recrystallised from light petroleum (bp 40-60 °C) to yield only the 2-isomer **7** as white crystals (3.30 g, 70%), mp 54-56 °C (lit.,[22] 55 °C); δ_H 9.55 (1H, s), 7.25-7.23 (4H, m), 7.15-7.13 (2H, m), 7.05-7.03 (2H, m), 6.38 (1H, m) and 2.41 (3H, s) (spectrum consistent with literature data[23]); δ_C 179.0, 138.1 (quat), 136.1 (quat), 132.5 (quat), 130.9, 129.6, 125.7, 121.5, 110.6 and 21.0; *m/z* 185 (M^+, 100 %), 157 (55), 128 (36) and 92 (83).

1-*p*-Tolylpyrrole-2-carbaldehyde *O*-methyloxime (8). A solution of 1-*p*-tolylpyrrole-2-carbaldehyde **7** (0.895 g, 4.8 mmol) and *O*-methylhydroxylamine hydrochloride (0.822 g, 9.7 mmol) in ethanol (50 cm^3) containing pyridine (0.767 g, 9.7 mmol) was heated under reflux for 1 h. Following standard work up the crude oxime ether was distilled to give 1-*p*-tolylpyrrole-2-carbaldehyde *O*-methyloxime **8**, bp 104-106 °C (0.5 Torr), that crystallised overnight to give a white solid (0.857 g, 83%), mp 52-53 °C (from hexane). (Found: C, 73.15; H, 6.65; N, 13.1. $C_{13}H_{14}N_2O$ requires C, 72.9; H, 6.55; N, 13.1 %); δ_H 7.88 (1H, s), 7.20 (4H, m), 6.88 (2H, m), 6.38 (1H, m), 4.04 (3H, s) and 2.42 (3H, s); δ_C 140.6, 137.8 (quat), 136.2 (quat), 135.8, 129.7, 126.2, 125.8, 123.6 (quat), 118.1, 62.1 and 20.8; *m/z* 214 (M^+, 28%), 91 (100) and 77 (72).

***N*-(Dimethylamino)pyrrole (9).** 2,5-Dimethoxytetrahydrofuran (11 g, 83 mmol) was added to a stirred solution of *N,N*-dimethylhydrazine (5 g, 83mmol) in acetic acid (15 cm^3) and heated at reflux for 2.5 h. The mixture was then quenched with sodium bicarbonate solution and extracted with dichloromethane (100 cm^3); the organic layer was washed with water (2 × 50 cm^3) and then brine (50 cm^3). The organic layer was then dried ($MgSO_4$) filtered and concentrated under vacuum. The residue was purified by distillation, bp 100-105 °C (15 Torr) [lit.,[24] 138-140 °C (767 Torr)], to give **9** as a pale yellow oil (4.9 g, 54%); □$_H$ 6.90 (2H, d, ^3J 2.2), 6.08 (2H, ^3J 2.2) and 2.87 (6H, s); δ_C 116.2 (2CH), 105.7 (2CH) and 48.3 ($2CH_3$).

***N*-(Dimethylamino)pyrrole-2-carbaldehyde (11).** *N,N*-Dimethylformamide (16.0 cm^3, 0.2 mol) was added to phosphorus oxychloride (16.2 cm^3, 0.2 mol) at 10 °C over a period of 15 min.[16] Dichloroethane was added while allowing the mixture to reach room temperature and stirring was continued for 10 min. A solution of the

pyrrole **9** (10 cm^3, 0.1 mol) in dichloroethane (80 cm^3) was added dropwise over 45 min while stirring at 10 °C. After heating under reflux for 1 h (95 °C) the reaction reached completion and a solution of sodium acetate (105 g) in water (210 cm^3) was added. After adding further water (50 cm^3), the aqueous layer was separated and extracted with dichloromethane (2 × 200 cm^3). The combined organic fractions were washed with saturated sodium carbonate solution, dried ($MgSO_4$), filtered and concentrated. Purification was carried out by dry flash column chromatography using a gradient from 100% hexane to a 50/50 mixture of hexane and ethyl acetate. Two products were isolated: *N*-(dimethylamino)pyrrole-2-carbaldehyde **11** (7.22 g, 52%), bp 115-120 °C (1.5 Torr) [lit.,[16] 84-86 °C (15 Torr)]; (Found: M^+ 138.0794. $C_7H_{10}N_2O$ requires *M* 138.0793); δ_H 9.76 (1H, s), 7.18 (1H, t, ^3J 2.5, ^4J 2.5), 6.91 (1H, dd, ^3J 4.3, ^3J 2.5) 6.20 (1H, dd, ^3J 4.3, ^4J 2.5) and 2.92 (6H, s); δ_C 179.0 (CH), 130.69 (quat) 124.0 (CH), 117.8 (CH), 108.2 (CH) and 47.2 ($2CH_3$); *m/z* 138 (M^+, 14%) and 94 (100): *N*-(dimethylamino)pyrrole-3-carbaldehyde (1.63 g, 12%), bp 148-150 °C (1.5 Torr); (Found: M^+ 138.0793. $C_7H_{10}N_2O$ requires *M* 138.0793); δ_H 9.75 (1H, s), 7.84 (1H, t, ^4J 2.0), 6.95 (1H, m), 6.63 (1H, t, ^4J 2.0) and 2.91 (6H, s); δ_C 184.6, 124.8, 123.1 (quat), 118.3, 106.0 and 47.6 ($2CH_3$); *m/z* 138 (M^+, 100%) and 94 (45).

***N*-(Dimethylamino)pyrrol-2-ylidene]-4-methylaniline (12).** *p*-Toluidine (155 mg, 1.45 mmol) was added to a suspension of $MgSO_4$ (300 mg) and *N*-(dimethylamino)pyrrole-2-carbaldehyde **11** (200 mg, 1.45 mmol) in toluene (10 cm^3) and the mixture was stirred at 90 °C for 75 min. The mixture was filtered and concentrated under vacuum before purifying by distillation to give a brown oil, which slowly solidified to give **12** (320 mg, 97%) (Found: M^+, 227.1420. $C_{12}H_{17}N_3$ requires *M* 227.1422); δ_H 8.62 (1H, s), 7.19-7.10 (5H, m), 6.85 (1H, dd, ^3J 4.1, ^4J 1.6), 6.25 (1H, dd, ^3J 4.2, 2.8, ^4J 0.5), 2.86 (6H, s) and 2.35 (3H, s); *m/z* 227 (M^+, 3%), 184 (67), 183 (100), 182 (34), 91 (31) and 65 (28).

***N*-(Dimethylamino)-2-(2-*p*-tolylvinyl)pyrrole (13).** Sodium hydride (103mg, 4.3 mmol) was added to toluene (12 cm^3) and stirred at 10 °C.[16] (4-Methylbenzyl)triphenylphosphonium bromide (1.86g, 4.3 mmol) was added followed by a second addition of sodium hydride (103mg, 4.3 mmol). This was stirred at 10 °C for 30 min, *N*-(dimethylamino)pyrrole-2-carbaldehyde **11** (0.50 g, 3.6 mmol) was added and the mixture was heated under reflux (125 °C) until completion of the reaction (3 h). After evaporation of solvent, the residue was taken up in water (50 cm^3) and extracted with dichloromethane (2 × 50 cm^3). The combined organic layers were dried ($MgSO_4$), filtered and the solvents evaporated. Purification by dry flash column chromatography, using hexane/ethyl acetate as eluent gave *N*-(dimethylamino)-2-(2-*p*-tolylvinyl)pyrrole **13** (64mg, 2.8mmol, 79%), mp 60-61 °C; (Found: M^+ 226.1469. $C_{15}H_{18}N_2$ requires *M* 226.1470); δ_H 7.42 (2H, d, ^3J 8.0), 7.27 (1H, d, ^3J 16.0), 7.16 (2H, d, ^3J 8.0), 7.00 (1H, m), 6.97 (1H, d, ^3J 16.0), 6.35 (1H, m), 6.21 (1H, m), 2.85 (6H, s) and 2.38 (3H, s); δ_C 136.4 (quat), 135.3 (quat), 130.8 (quat), 129.1 (2CH), 125.8 (2CH), 125.1, 116.2, 113.4, 107.6, 102.03, 47.7 ($2CH_3$) and 21.1 (CH_3); *m/z* 226 (M^+, 73%) and 183 (100).

***N*-(Dimethylamino)-3-(2-*p*-tolylvinyl)pyrrole (15).** Synthesised as above for **13**, from *N*-(dimethylamino)-pyrrole-3-carbaldehyde **14** in 60% yield, *N*-(dimethylamino)-3-(2-*p*-tolylvinyl)pyrrole **15** had mp 70 °C; (Found: M^+ 226.1469. $C_{15}H_{18}N_2$ requires *M* 226.1470); δ_H 7.34 (2H, d, ^3J 8.1), 7.13 (2H, d, ^3J 8.1), 6.97 (1H, m), 6.94 (1H, d, ^3J 16.5), 6.84 (1H, t, ^3J 2.8), 6.75 (1H, d, ^3J 16.5), 6.31 (1H, t, ^3J 2.8), 2.85 (6H, s) and 265 (3H, s); δ_C 136.0 (quat), 135.4 (quat), 129.1 (2CH), 125.51 (2CH), 124.2 (CH), 121.2 (CH), 120.5 (quat), 117.8 (CH), 115.6 (CH), 103.1 (CH), 48.2 ($2CH_3$) and 21.0 (CH_3); *m/z* 226 (M^+, 100%) and 167 (66).

Flash Vacuum Pyrolysis Experiments

Conditions for the pyrolyses were established in small scale experiments in which the products were dissolved in a deuteriated solvent and analysed immediately by ^1H NMR spectroscopy. On a larger scale the crude products were separated by flash column chromatography unless otherwise stated. The conditions [precursor

quantity, furnace temperature (T_f), inlet temperature (T_i), pressure range (P), and pyrolysis time (t)] are provided individually for each reaction.

FVP of 1-*p*-tolylpyrrole-2-carbaldehyde *O*-methyloxime (8). FVP of 1-*p*-tolylpyrrole-2-carbaldehyde-*O*-methyloxime **8** was carried out on 0.1 mmol (25 mg) scale to identify the optimum conditions (T_i 75-105 °C, T_f 500-650 °C, P 1.8 × 10^{-2} Torr, 20 min). The composition of the resulting mixture showed: 500 °C, 15% of **8** converted, 550 °C, 43%; 575 °C, 71%; 600 °C, 90%; 650 °C, 94%. Formation of the iminyl was essentially complete at 650 °C and this temperature was chosen for preparative pyrolysis.

Thus, FVP of **8** [0.437 g (2.0 mmol), T_i 75-105 °C, T_f 650 °C, P 1.2 × 10^{-2} Torr, t 30 min] provided 7-methylpyrrolo[1,2-*a*]quinoxaline **16** (0.172 g, 40%) (Found: 182.08442; $C_{12}H_{10}N_2$ requires *M*, 182.08440); δ_H 8.77 (1H, s), 7.88-7.71 (3H, m), 7.32 (1H, m), 6.87-6.85 (2H, m) and 2.48 (3H, s); δ_C 145.5, 135.4 (quat), 134.9 (quat), 129.7, 128.8, 126.2 (quat), 125.7 (quat), 113.9, 113.7, 113.4, 107.0 and 21.0 (spectra consistent with literature data[25]); *m/z* 182 (M^+, 100%), 127 (7) and 90 (14): 8-methylpyrrolo[1,2-*a*]quinoxaline **17** (0.175 g, 41%) (Found: 182.0843. $C_{12}H_{10}N_2$ requires *M*, 182.0844); δ_H 8.74 (1H, s), 7.91 (1H, m), 7.87 (1H, d, ^3J 8.2), 7.68 (1H, s), 7.29 (1H, dd, ^3J 8.2, ^4J 0.6), 6.90-6.88 (2H, m) and 2.58 (3H, s); δ_C 144.7, 138.2 (quat), 133.5 (quat), 129.5, 128.8 (quat), 127.6 (quat), 126.3, 113.8, 113.7, 113.4, 106.9 and 21.6; *m/z* 182 (M^+, 100%), 91 (10) and 63 (4): 1-*p*-tolylpyrrole-2-carbonitrile **18** (0.028 g, 8%) (Found: 182.0842. $C_{12}H_{10}N_2$ requires *M*, 182.0844); δ_H 7.34-7.28 (4H, m), 7.04 (1H, m), 6.97 (1H, m), 6.32 (1H, m) and 2.41 (3H, s); δ_C 138.3 (quat), 135.6 (quat), 130.0, 126.8, 123.9, 121.8, 113.8 (quat), 110.3, 103.9 and 20.9 (spectra consistent with literature data[26]); *m/z* 182 (M^+, 100%), 91 (14) and 65 (9): 1-*p*-tolylpyrrole **6** (0.018 g, 5%), δ_H 7.30-7.18 (4H, m), 7.05 (2H, t, ^3J and ^4J 2.2), 6.34 (2H, t, ^3J and ^4J 2.2) and 2.37 (3H, s); δ_C 138.3 (quat), 135.2 (quat), 129.9, 120.4, 119.3, 109.9 and 20.7 [spectra consistent with those of an authentic sample (see earlier Experimental details)].

FVP of *N*-(dimethylamino)pyrrole 9 – temperature profile. Due to its low boiling point (138-140 °C at atmospheric pressure) *N*-(dimethylamino)pyrrole **9** was frozen in the inlet system using an acetone/dry ice bath which remained in place around the inlet as the vacuum was applied. The cooling bath was then slowly removed allowing the *N*-(dimethylamino)pyrrole **9** to volatilise into the furnace tube in a controlled manner.

***T*f 550 °C**, (24.8 mg, T_i RT, *P* 2.3-2.4 × 10^{-2} Torr, *t* 16 min) gave *N*-(dimethylamino)pyrrole **9** (*ca* 97%)

***T*f 600 °C**, (21.5 mg, T_i RT, *P* 2.4-3.0 × 10^{-2} Torr, *t* 17 min) gave *N*-(dimethylamino)pyrrole **9** (*ca* 92%) and pyrrole **10** (*ca* 8%)

***T*f 650 °C**, (21.3 mg, T_i RT, *P* 2.6-3.5 × 10^{-2} Torr, *t* 16 min) gave *N*-(dimethylamino)pyrrole **9** (*ca* 63%) and pyrrole **10** (*ca* 37%)

***T*f 700 °C**, (21.6 mg, T_i RT, *P* 2.6-3.2 × 10^{-2} Torr, *t* 15 min) gave *N*-(dimethylamino)pyrrole **9** (*ca* 21%) and pyrrole **10** (*ca* 79%)

***T*f 750 °C**, (24.3 mg, T_i RT, *P* 2.8-5.0 × 10^{-2} Torr, *t* 17 min) gave *N*-(dimethylamino)pyrrole **9** (*ca* 18%) and pyrrole **10** (*ca* 82%)

***T*f 800 °C**, (24.6 mg, T_i RT, *P* 2.5-6.0 × 10^{-2} Torr, *t* 16 min) gave *N*-(dimethylamino)pyrrole **9** (*ca* 3%) and pyrrole **10** (*ca* 97%)

***T*f 850 °C**, (25.5 mg, T_i RT, *P* 3.2-7.3 × 10^{-2} Torr, *t* 19 min) gave pyrrole **10** (*ca* 99%).

F**VP of *N*-[dimethylamino)pyrrol-2-ylidene]-4-methylaniline (12).** FVP of *N*-[dimethylamino)pyrrol-2-ylidene]-4-methylaniline **12** [(20 mg, 0.1 mmol), T_i 74-106 °C, T_f 800 °C, 1.6 × 10^{-2} Torr, 45 min] gave a mixture of only 7-methylpyrrolo[1,2-*a*]quinoxaline **16** and 8-methylpyrrolo[1,2-*a*]quinoxaline **17** in a 1:3 ratio (27% of **16** : 73% of **17**) (spectroscopic data as above).

FVP of *N*-(dimethylamino)-2-(2-*p*-tolylvinyl)pyrrole (13). FVP of *N*-(dimethylamino)-2-(2-*p*-tolylvinyl)pyrrole **13** [108 mg (0.48 mmol) T_f 750 °C, T_i 140 °C, *P* 2.6-14 × 10^{-2} Torr, *t* 1 h) gave 8-methylpyrrolo[1,2-*a*]quinoline **19** (43 mg, 50%), (Found: M^+ 181.0891. $C_{13}H_{11}N$ requires *M* 181.0892); δ_H 7.71 (1H, s, H-8), 7.54 (1H, d, ^3J 7.9,

H-6), 7.34 (1H, m, H-1), 7.27 (1H, d, ^3J 9.3, H-4), 7.15 (1H, d, ^3J 7.9, H-7), 6.97 (1H, d, ^3J 9.3, H-5), 6.80 (1H, t, ^3J 3.2, H-2), 6.52 (1H, m, H-3) and 2.56 (3H, s, Me); δ_C 137.9 (quat), 133.2 (quat), 131.0 (quat), 128.2, 124.7, 121.3 (quat), 118.5, 117.8, 114.2, 112.4, 111.5, 102.2 and 21.8 (Me); *m/z* 181 (M^+, 100%).

FVP of *N*-dimethylamino-3-(2-*p*-tolylvinyl)pyrrole (15). FVP of *N*-dimethylamino-3-(2-*p*-tolylvinyl)pyrrole **15** [116 mg (0.51 mmol) T_f 750 °C, T_i 140 °C, *P* 2.1-10 × 10^{-2} Torr, t 1 h) gave a mixture of products: 8-methylpyrrolo[1,2-*a*]quinoline **19** (4.6 mg, 5%); δ_H 7.71 (1H, s), 7.54 (1H, d, ^3J 7.9), 7.34 (1H, m), 7.27 (1H, d, ^3J 9.3), 7.15 (1H, d, ^3J 7.9), 6.97 (1H, d, ^3J 9.3), 6.80 (1H, t, ^3J 3.2), 6.52 (1H, m) and 2.56 (3H, s): 3-(2-*p*-tolylvinyl)pyrrole **20** (10.3 mg, 11%) (Found: M^+ 183.1047. $C_{13}H_{13}N$ requires *M* 183.1048); δ_H 8.16 (1H, br. s), 7.37 (2H, d, ^3J 8.1), 7.15 (2H, d, ^3J 8.1), 7.04 (1H, d, ^3J 16.2), 6.90 (1H, dd, ^3J 4.2), 6.81 (1H, d, ^3J 16.2), 6.80 (1H, dd, ^4J 2.6), 6.51 (1H, dd, ^3J 4.2, ^4J 2.6) and 2.36 (3H, s); δ_C 136.04 (quat), 135.40 (quat), 129.12 (2CH), 125.56 (2CH), 124.60 (CH), 123.10 (quat), 121.20 (CH), 119.01 (CH), 117.12 (CH), 105.45 (CH) and 20.82 (CH_3) (spectra consistent with literature data[27]); *m/z* 183 (M^+, 100%): a fraction which was tentatively identified as impure 8-methylbenzo[*g*]indole **S1** (trace) (Found: M^+ 181.0891. $C_{13}H_{11}N$ requires *M* 181.0892); δ_H 9.01 (1H, br. s), 7.85-7.80 (2H, m), 7.67 (1H, d, ^3J 8.5), 7.49 (1H, d, ^3J 8.5), 7.36-7.13 (2H, m), 6.12 (1H, m) and 2.39 (3H, s); *m/z* 181 (M^+, 100%) and 84 (92).

Formation of products from FVP of *N*-dimethylamino-3-(2-*p*-tolylvinyl)pyrrole (15). Three products were isolated, in low yield, from FVP of **15**. The product of hydrogen-capture by the pyrrol-1-yl radical, **20**, retains the carbon skeleton of the precursor. Similarly, the formation of 8-methylbenzo[*g*]indole **S1**, tentatively identified in trace amounts from an impure fraction, is consistent with delocalisation of the pyrrol-1-yl radical to the 2-position, followed by cyclisation. Clearly this is not a favourable process for the initial radical. Finally the formation of 8-methylpyrrolo[1,2-*a*]quinoline **19** requires rearrangement of the vinyl group from the 3-position to the 2-position of the pyrrole, followed by cyclisation. Such 1,5-shifts are well-known in the thermal chemistry of pyrroles,[15] and although the rearrangement is not normally quantitative at temperatures as low as 750 °C in our apparatus, they may well account for the formation of such a minor product (5%).

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Supplementary Material

Results of DFT calculations are available in the Supplementary Material file associated with this paper.

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