The Thermolysis of Polyazapentadienes. Part 5.[1,2] Degenerate Rearrangement of Aryliminoiminyl Radicals: A ^{15}N-Labelling Study

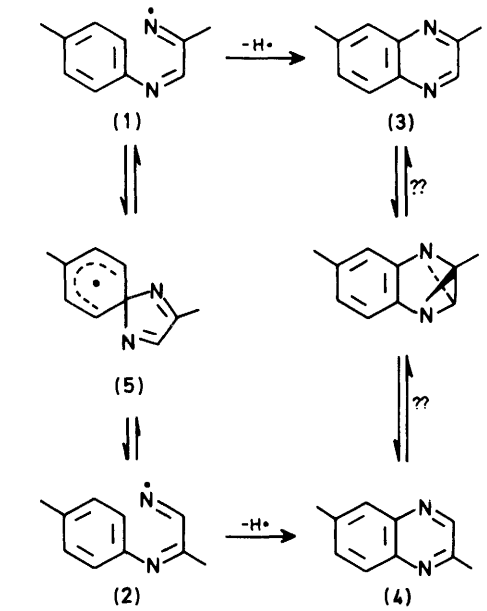
Hamish McNab * and Graeme S. Smith
Department of Chemistry, University of Edinburgh, West Mains Road, Edinburgh EH9 3JJ

The ^{15}N n.m.r. spectra of 5- and 6-methylquinoxaline are unambiguously interpreted by the synthesis and spectra of specifically ^{15}N-labelled quinoxalines. The results are compared with the ^{13}C n.m.r. spectra of analogous naphthalenes. Pyrolysis of [2-^{15}N]- or [5-^{15}N]-1-phenyl-5-*p*-tolyl-1,2,5-triazapentadiene gives an unequal mixture of [1-^{15}N]- and [4-^{15}N]-6-methylquinoxaline owing to equilibration of the intermediate aryliminoiminyl radical *via* a spirodienyl radical to the extent of *ca.* 88%. 5- and 6-Methylquinoxaline obtained from the [2-^{15}N]-5-*m*-tolyl analogue show evidence of rearrangement to the extent of 72 and 80% respectively while the distribution of label in 5-methylquinoxaline obtained from the corresponding [2-^{15}N]-5-(2,6-dimethylphenyl) compound suggests almost complete involvement of the spirodienyl in this case.

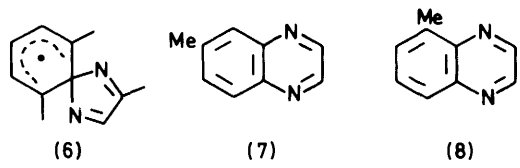
Mixtures of quinoxalines are formed when *C*-methyl aryliminoiminyl radicals are generated at high temperatures in the gas phase. For example, the quinoxalines (3) and (4) are both produced from the radical (1) or (2), and these results have been interpreted in terms of a rearrangement *via* an intermediate spirodienyl radical (5) (Scheme 1).[3,4] Since the ratio (3) : (4) is dependent on the position of the *C*-methyl group in the precursor radical, it was proposed that direct cyclisation could compete with this radical rearrangement. In order to evaluate quantitatively the contribution of the two mechanisms, it was necessary to assume that the migration tendencies of the two nitrogen atoms of the radical (5) were equal,[4] an assumption which was later shown to be invalid for the related spirodienyl radical (6).[1] In addition, it was not possible to exclude conclusively an alternative mechanism, which involves exchange at the carbon centres C(2) and C(3) of the quinoxalines,[3] *e.g. via* a benzvalene intermediate (Scheme 1) for which there is ample precedent in other systems.[5]

These mechanistic ambiguities are due to the use of a methyl group as a label which destroys the symmetry of the spirodienyl, and to the presence of the label on C(2) or C(3). In this paper we report the resolution of these difficulties by the use of isotopic labelling at the nitrogen atoms. Such experiments are now particularly attractive because of the availability of ^{15}N n.m.r. techniques,[6] for analysis of the products; the large chemical shift range and narrow linewidth characteristics of ^{15}N n.m.r. spectra should in theory allow resolution of closely similar nitrogen atoms. In addition, it is possible to work at low levels of ^{15}N enrichment, and still preserve a large excess over natural abundance (*e.g.* 5% excess of ^{15}N represents *ca.* 14 times natural abundance).

The ^{15}N n.m.r. spectra of 6-methylquinoxaline (7) and 5-methylquinoxaline (8), recorded at natural abundance in [$^2H_6$]benzene, each show two well resolved signals [(7), δ † −52.13 and −52.85 p.p.m.; (8), δ −49.64 and −54.14 p.p.m.]. In order to assign these signals unambiguously, samples of the specifically labelled quinoxalines (7*) and (8*) were synthesised using the five step sequence of Scheme 2. Key steps include the direct synthesis of the amide (11) from labelled ammonium salt,[7] the generation of the amine (12) by the Hofmann reaction,[8] and the clean formation of the diamine (13) by catalysed sodium borohydride reduction.[9] Because of some variation of chemical shift due to concentration effects, the spectra were accumulated until the minor (natural abundance) peak was clearly visible above the noise level [(7*), δ −51.19 (minor peak) and −51.95 (major peak) p.p.m.; (8*), δ −49.71 (major peak) and −54.31 (minor peak) p.p.m.]. Hence the signals were assigned as shown in the Figure, where comparison is also made with the corresponding ^{13}C n.m.r. chemical shifts of 1- and 2-methylnaphthalenes.[10]

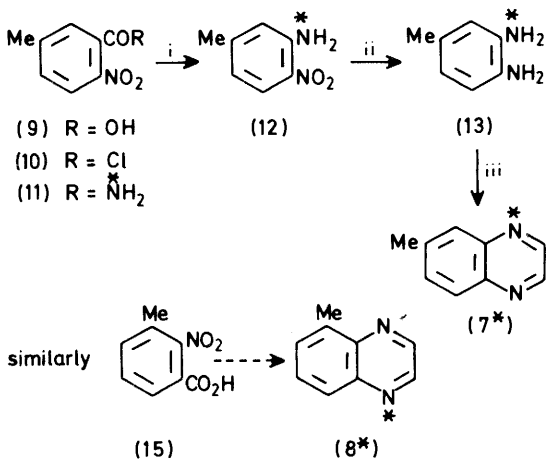


Scheme 1.



The ^{15}N and ^{13}C n.m.r. data show remarkable consistency. A methyl group in the α′-position causes a much greater separation of the signals than the substituent in the β′-position. For these 1(5)-substituted compounds, the α-site closer to the substituent in the adjacent ring is shielded relative

† All ^{15}N n.m.r. chemical shifts reported in this paper are quoted with reference to external nitromethane. Positive shifts are to high frequency.



Scheme 2. Asterisks denote a ^{15}N label. *Reagents:* i, NaOBr; ii, $NaBH_4$, Pd–C; iii, glyoxal

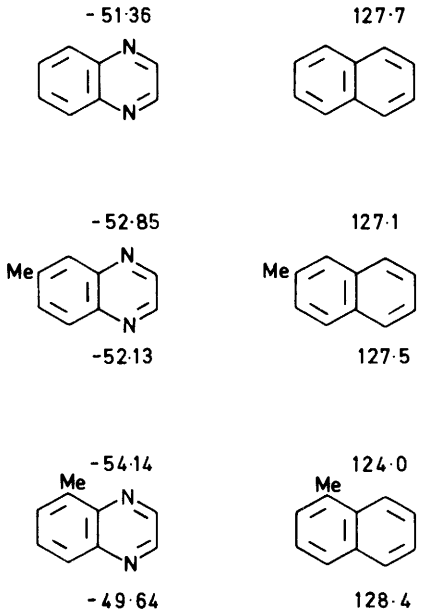
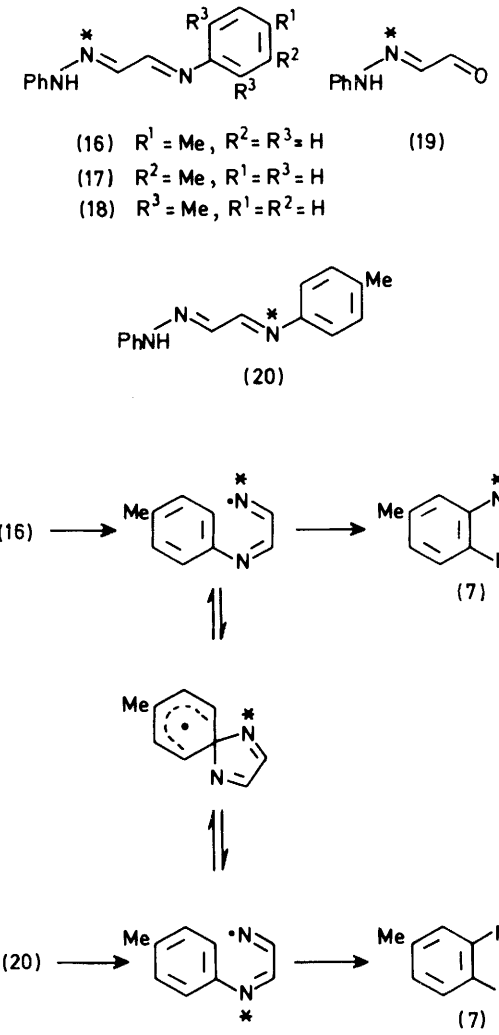


Figure. Chemical shifts of α-positions in quinoxalines and naphthalenes

to that in the unsubstituted quinoxaline or naphthalene, while the other α-site is deshielded, though to a smaller extent. 2(6)-Substitution by a methyl group causes a low frequency shift of both α-sites in the adjacent ring, though the effect is small. It seems likely, therefore, that the ^{15}N and ^{13}C chemical shifts are being influenced by similar factors, and that in these systems the ^{15}N n.m.r. spectra may be assigned *to a first approximation* from the considerable data on naphthalenes.[10–12]

The iminyl precursors (16)—(18) were synthesised by standard methods [13,14] from labelled glyoxal phenylhydrazone (19).[15] The required [2-^{15}N]phenylhydrazine was made by diazotisation of aniline with sodium [^{15}N]nitrite, followed by reduction.[16] In order to assess the accuracy of the methods it was necessary to obtain a [5-^{15}N]-precursor for comparison. Hence compound (20) [*cf.* (16)] was made by reaction of unlabelled glyoxal phenylhydrazone with [^{15}N]-*p*-toluidine, which itself was synthesised *via* the Hofmann reaction as above. The iminyl radicals were generated by gas-phase pyrolysis at 650 °C as previously reported,[13,14] and the entire

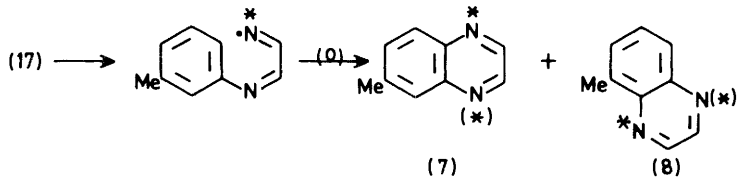


Scheme 3.

pyrolysate was examined by ^{15}N n.m.r. (generally over the range 0 to −80 p.p.m.) without purification or isolation of the quinoxaline. No significant peaks other than those of the quinoxaline(s) were observed in this range.

Pyrolysis of compound (16) gave a dark coloured pyrolysate, whose ^{15}N n.m.r. spectrum showed *two* peaks as expected for 6-methylquinoxaline [δ −51.72 (minor peak) and −52.50 (major peak) p.p.m.]. This result clearly eliminates interconversion *via* the benzvalene-type intermediate as the sole isomerisation mechanism, since this route does not interchange the position of the nitrogen atoms. The major peak corresponds to N(4), which confirms earlier [3,4] speculation that direct cyclisation might compete with equilibration *via* the spirodienyl radical (Scheme 3). As expected, entry into the energy surface by the alternative route from (20) (Scheme 3) again gave 6-methylquinoxaline [δ −52.98 (major peak) and −53.72 (minor peak) p.p.m.] though in this case the major peak is due to N(1).

The high symmetry of the system illustrated by Scheme 3 allows a good estimate of the accuracy achieved in quantification of the reaction paths of direct and spirodienyl cyclisations. Computer calculated ' integral ' and ' intensity ' values showed relatively low consistency [*e.g.* from (16), integral ratio 0.88 : 1; from (20), integral ratio 1 : 0.64] due to high levels. However, simple triangulation of expanded (0.2 p.p.m. cm^{-1}) spectra gave results which are probably accurate to



Scheme 4.

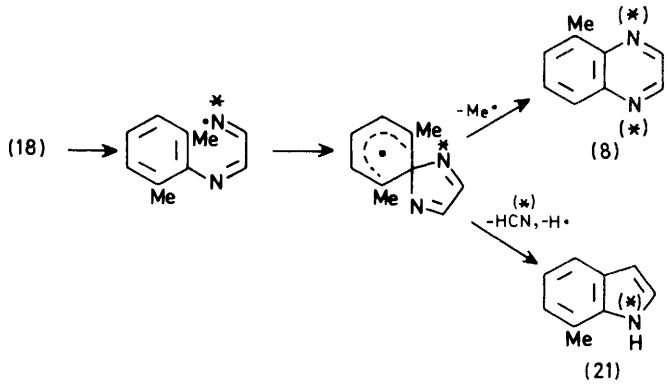
within ±5% [from (16), peak ratio 0.75 : 1, from (20), peak ratio 1 : 0.82]. Application of the earlier [3] formula therefore gives a spirodienyl component of 88% of the total reaction pathway, with a 12% leakage to product by direct cyclisation.

The possibility of a $^{15}N/^{14}N$ isotope effect [17] has been neglected in the above analysis. In related systems, such effects at ambient temperature amount to less than 3%, and would be expected to be much lower at high temperature; [17] any contribution is therefore well within the estimated accuracy of the data.

Pyrolysis of the *m*-tolyl compound (17) gives a mixture of 6- and 5-methylquinoxaline and indeed four lines are found in the ^{15}N n.m.r. spectrum of the pyrolysate (Scheme 4) [(7), δ −51.12 and −51.92 p.p.m., peak ratio 1 : 0.67; (8), δ −49.61 and −53.41 p.p.m., peak ratio 0.56 : 1]. The spirodienyl route therefore accounts for 80 and 72% respectively of the reaction. To a slight extent, the direct cyclisation seems to be relatively favoured in this case, possibly because of a slight activating effect of the methyl group to *ortho* and *para* attack by the free radicals.[18]

In contrast, earlier results in the *C*-methyl series [1,2] suggested that the spirodienyl mechanism dominated the cyclisation of 2,6-dimethylphenyliminoiminyl radicals. Indeed, the 5-methylquinoxaline obtained by pyrolysis of (18) was almost equally labelled at both nitrogen atoms [δ −51.62 and −54.37 p.p.m., peak ratio 1 : 0.96], corresponding to a spirodienyl component of 98%.* The spirodienyl pathway in this case is favoured by the activating effect of the two *ortho* methyl groups to the radical attack at the 1-position,[18] whilst the direct cyclisation is disfavoured by the steric effects of these groups.

The chemical shift values in this case are different from those of the authentic material owing to the presence of (labelled) 7-methylindole (21) (δ −252.83: lit.,[6] δ −247.3 p.p.m.) which can apparently act as a shift reagent in n.m.r. spectroscopy.[1] Further, the retention of the ^{15}N label in this compound confirms the spirodienyl mechanism [1] for its formation (Scheme 5).



Scheme 5.

Experimental

Ether refers to diethyl ether.

The sodium [^{15}N]nitrite and [^{15}N]ammonium nitrate had 6.7 and 5.6% excess of ^{15}N respectively.

[4-^{15}N]-6-*Methylquinoxaline*.—(*a*) [1-^{15}N]-5-*Methyl*-2-*nitrobenzamide*.[7] A solution of [^{15}N]ammonium nitrate (1.87 g, 23 mmol) and sodium hydroxide (1.96 g, 49 mmol) in water (25 ml) was added to a solution of redistilled 5-methyl-2-nitrobenzoyl chloride (5 g, 25 mmol) (obtained in 70% yield from the corresponding acid and thionyl chloride) in chloroform (175 ml). The mixture was shaken for 1 h at room temperature after which the solid amide was filtered off. The chloroform layer of the filtrate was separated, dried (Na_2SO_4), and concentrated to give a further crop of product. The total yield was 3.62 g (86%, with respect to ammonium nitrate), m.p. 174—176 °C (lit.,[19] 176—177 °C).

(*b*) [1-^{15}N]-5-*Methyl*-2-*nitroaniline*.[8] The above amide (3.62 g, 20 mmol) was added to a solution of sodium hypobromite [from bromine (1.2 ml), sodium hydroxide (4.8 g), and water (40 ml)]. The reaction proceeded with evolution of heat, and was completed by heating the mixture at 70 °C for 20 min. On cooling, the required amine crystallised, and was purified by recrystallisation from ethanol (1.68 g, 55%), δ($CDCl_3$) 7.96 (1 H, d), 6.58 (1 H, s), 6.45 (1 H, dd), 6.0 (2 H, br s), and 2.26 (3 H, s).

(*c*) [3-^{15}N]-3,4-*Diaminotoluene*.[9] A solution of the above nitroaniline (1.68 g, 11.1 mmol) in methanol (33 ml) was added dropwise, with stirring, to a suspension of palladium on charcoal (10%, 55 mg) in a solution of sodium borohydride (0.86 g, 23 mmol) in water (20 ml). The stirring was continued for a further 30 min, after which the solution was acidified (dil. hydrochloric acid) and then made basic with dilute sodium hydroxide solution. The catalyst was filtered off, and the filtrate was extracted with ether (4 × 15 ml). The organic extracts were dried (Na_2SO_4) and concentrated to give the diamine (1.09 g, 64%), m.p. 86—88 °C (lit.,[20] 89—90 °C).

(*d*) [4-^{15}N]-6-*Methylquinoxaline*. The above diamine (0.86 g, 0.70 mmol) was suspended in hot water (12 ml) and added to a warm mixture of glyoxal (40%, 0.85 ml) and sodium disulphite (1.56 g) in water (8 ml). After 15 min at room temperature, the mixture was basified with a solution of sodium carbonate (3.3 g) in water (8 ml) and extracted with ether (3 × 25 ml). The organic extracts were dried (Na_2SO_4), concentrated, and distilled (Kugelrohr) to give the quinoxaline (0.49 g, 48%), b.p. 125 °C (12 Torr) [lit.,[21] 118—120 °C (16 Torr)].

[1-^{15}N]-5-*Methylquinoxaline*.—This compound was prepared by a similar sequence to that described for the 6-methyl derivative. The yields of the individual steps were as follows: 3-methyl-2-nitrobenzoyl chloride (69%) (from the carboxylic

* This value differs from that reported in the preliminary communication,[2] owing to the use of triangulation rather than peak integral ' values.

acid); [1-^{15}N]-3-methyl-2-nitrobenzamide (64%, with respect to the enriched ammonium nitrate) (from the acid chloride); [1-^{15}N]-3-methyl-2-nitroaniline (21%) (from the amide); [3-^{15}N]-2,3-diaminotoluene (65%) (from the nitroaniline); [1-^{15}N]-5-methylquinoxaline (77%) (from the diaminotoluene), b.p. 140—143 °C (20 Torr) [lit.,[22] 120 °C (15 Torr)].

[2-^{15}N]*Phenylhydrazine*.—This compound was made by diazotisation of aniline with sodium [^{15}N]nitrite, followed by reduction of the diazonium salt with stannous chloride in concentrated hydrochloric acid.[16] The base was liberated from the salt by treatment with sodium hydroxide, and was purified by Kugelrohr distillation at 120 °C (16 Torr). The yield was 51% with respect to sodium nitrite.

[2-^{15}N]*Glyoxal Monophenylhydrazone*.—Prepared by the standard method in 87% yield by reaction of the above hydrazine with aqueous glyoxal,[15] this compound was used without purification in the preparation of the triazapentadienium salts.

[2-^{15}N]-5-*Aryl*-1-*phenyl*-1,2,5-*triazapentadienium Salts and Their Bases*.—The salts were obtained from the above hydrazone, and the appropriate arylammonium perchlorate in ethanol.[13] The yields obtained were as follows: 5-*p*-tolyl (57%); 5-*m*-tolyl (54%); and 5-(2,6-dimethylphenyl) (63%). The corresponding bases were obtained from the salts by the use of potassium hydroxide in methanol:[14] the yields were 82, 90, and 92% respectively.

[1-^{15}N]-p-*Toluidine*.—[1-^{15}N]-*p*-Toluamide (4.0 g, 30 mmol) was subjected to Hofmann degradation under standard conditions.[8] The [1-^{15}N]amine was obtained in 54% yield after steam distillation, m.p. 39—40 °C (lit.,[23] 44 °C).

[5-^{15}N]-1-*Phenyl*-5-p-*tolyl*-1,2,5-*triazapentadiene* (cf. *Ref.* 15).—Reaction of glyoxal monophenylhydrazone (1.48 g, 10 mmol) with [1-^{15}N]-*p*-toluidine (1.07 g, 10 mmol) in toluene (100 ml) for 24 h gave the triazapentadiene as yellow crystals. A second crop was obtained by concentration of the filtrate. The total yield was 2.29 g (97%).

Pyrolysis Experiments.—The apparatus and general techniques were as previously reported,[13] and the conditions are quoted as follows: triazapentadiene, quantity pyrolysed, inlet temperature, furnace temperature, pressure range, pyrolysis time, and residue in the inlet. The entire pyrolysate was dissolved in [$^2H_6$]benzene and a trace of chromium tris(acetylacetonate) was added for the ^{15}N n.m.r. studies, which are reported in detail in the Discussion section.

[2-^{15}N]-1-Phenyl-5-*p*-tolyl-1,2,5-triazapentadiene (0.81 g, 3.5 mmol), 190 °C, 650 °C, 3—20 × 10^{-3} Torr, 1 h (residue 11%).

[2-^{15}N]-Phenyl-5-*m*-tolyl-1,2,5-triazapentadiene (0.83 g, 3.5 mmol), 120 °C, 650 °C, 5—10 × 10^{-3} Torr, 1.25 h (residue 30%).

[2-^{15}N]-5-(2,6-Dimethylphenyl)-1-phenyl-1,2,5-triazapentadiene (1.00 g, 4 mmol), 145 °C, 650 °C, 1—20 × 10^{-3} Torr, 1.25 h (residue 22%).

[5-^{15}N]-1-Phenyl-5-*p*-tolyl-1,2,5-triazapentadiene (1.81 g, 7.6 mmol), 190 °C, 650 °C, 2—20 × 10^{-3} Torr, 1 h (residue 19%).

Acknowledgements

We are most grateful to Dr. I. H. Sadler and Dr. D. Reed for the ^{15}N n.m.r. spectra, and for helpful discussions.

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Received 2nd *August* 1983; *Paper* 3/1362