(1α and 1β)Methyl-1,1a,2,3,4,5-hexahydro-11*H*-azirino-[1′2′:2,3][1,2]diazocino[8,1-*b*]quinazolin-11-one: Preference for a *trans*-Fused Aziridine in an Eight-membered Ring

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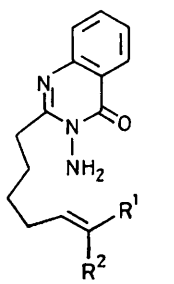
Intramolecular trapping of the nitrenes from oxidation of *cis*- and *trans*-2-(hept-2-en-7-yl)-3-amino-quinazolinones (**1**) and (**3**) gives the aziridines (**2**) and (**4**) respectively; in solution at room temperature (**4**) contains a mixture of nitrogen invertomers with the major invertomer having a *trans*-aziridine ring fusion, the latter being the only form present in the crystalline state.

As part of a programme having as its goal a description of the preferred transition state geometry for singlet nitrene addition to alkenes, we have been studying the intramolecular additions of *N*-nitrenes.

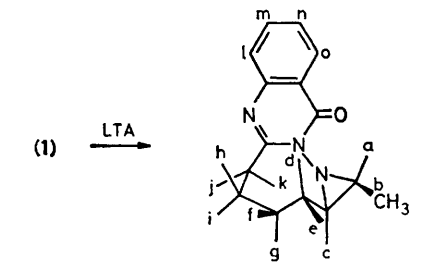
Oxidation of the *N*-aminoquinazolinone (**1**), m.p. 60—61 °C with lead tetra-acetate (LTA) in dichloromethane by simultaneous addition of (**1**) and LTA to minimise de-amination[1] gave the crystalline aziridine (**2**), m.p. 159—160 °C (37%, isolated).

N.m.r. analysis of (**2**) at 400 MHz gives δ($CDCl_3$) 8.19 (H_o, ddd, J_{ol} 0.7, J_{om} 1.5, J_{on} 8.1 Hz), 7.68 (H_m, ddd, J_{mo} 1.5, J_{mn} 7.0, J_{ml} 8.1 Hz), 7.60 (H_l, ddd, J_{lo} 0.7, J_{ln} 1.3, J_{lm} 8.1 Hz), 7.40 (H_n, ddd, J_{nl} 1.3, J_{nm} 7.0, J_{no} 8.1 Hz), 3.29 (H_k, ddd, J_{kl} 1.1, J_{kh} 11.7, J_{kj} 13.3 Hz), 2.92 (H_j, ddd, J_{jh} 1.1, J_{ji} 8.3, J_{jk} 13.3 Hz), 2.43 (H_a, dt, J_{ab} 5.5, J_{ac} 5.7 Hz), *ca.* 2.37 (H_c, ddd, J_{ce} 1.5, J_{ca} 5.7, J_{cd} 12.2 Hz), *ca.* 2.36 (H_i, ddddd, J_{if} 1.1, J_{ik} 1.1, J_{ig} 6.0, J_{ij} 8.3, J_{ih} 14 Hz), 2.28 (H_e, ddddd, J_{eg} 1.3, J_{ec} 1.5, J_{ef} 6.0, J_{ed} 15.9 Hz), *ca.* 1.95 (H_f, ddddd, J_{fi} 1.1, J_{fd} 1.3, J_{fh} 5.9, J_{fe} 6.0, J_{fg} 15 Hz), 1.93 (H_h, ddddd, J_{hj} 1.1, J_{hf} 5.9, J_{hk} 11.7, J_{hg} 13, J_{hi} 14 Hz), 1.68 (H_g, ddddd, J_{ge} 1.3, J_{gi} 6.0, J_{gd} 10.2, J_{gh} 13, J_{gf} 15 Hz), 1.58 (3 × H_b, d, J_{ba} 5.5 Hz), 0.92 (H_d, dddd, J_{df} 1.3, J_{dg} 10.2, J_{dc} 12.2, J_{de} 15.9 Hz). These data suggest that the eight-membered ring in (**2**) is rigid or at least heavily biased towards the twist-boat-chair[2] conformation shown.

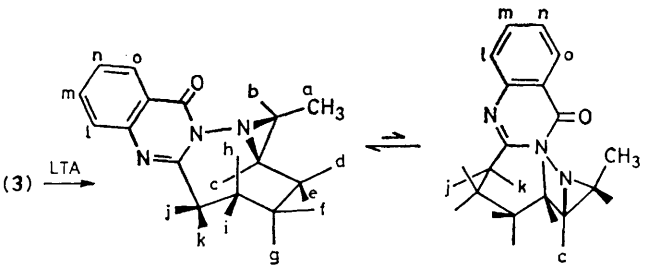


(**1**) R^1 = Me, R^2 = H
(**3**) R^1 = H, R^2 = Me

Oxidation of (**3**), m.p. 79—80 °C, gives a different aziridine from (**2**) and examination of the crude reaction mixture by n.m.r. spectroscopy indicates that (**2**) is completely absent, *i.e.* nitrene addition to the *cis*-double bond is stereospecific.[3]



(2)



(4a) (4b)

The 400 MHz spectrum of this crystalline aziridine, m.p. 118—119 °C (18%, isolated), from the oxidation of (**3**) shows that it is a mixture of invertomers at nitrogen (**4a**) and (**4b**) in the ratio 5:1 with the signals from the major invertomer at δ($CDCl_3$) 8.19 (H_o, dd, J_{om} 1.7, J_{on} 8.0 Hz), 7.66 (H_m, ddd, J_{mo} 1.7, J_{mn} 7.0, J_{ml} 8.2 Hz), 7.56 (H_l, dd, J_{ln} 1.1, J_{lm} 8.2 Hz), 7.40 (H_n, ddd, J_{nl} 1.1, J_{nm} 7.0, J_{no} 8.0 Hz), 3.51 (H_k, ddd, J_{kh} 1.8, J_{kl} 10.9, J_{kj} 17.3 Hz), 3.08 (H_j, ddd, J_{jl} 1.2, J_{jh} 8.1, J_{jk} 17.3 Hz), 2.83 (H_b, td, J_{ba} 6.0, J_{bc} 8.1 Hz), 2.52 (H_c, ddd, J_{ce} 2.4, J_{cb} 8.1, J_{cd} 12.0 Hz), 2.37 (H_h, ddddd, J_{hf} 1.7, J_{hk} 1.8, J_{hj} 8.1, J_{hg} 12.1, J_{hl} 15.2 Hz), 2.12 (H_f, ddddd, J_{fh} 1.7, J_{fe} 2.6, J_{fl} 6.8, J_{fd} 7.1, J_{fg} 14 Hz), *ca.* 2.02 (H_i, ddddd, J_{ig} 1.2, J_{ij} 1.2, J_{if} 6.8, J_{ik} 10.9, J_{ih} 15.2 Hz), 2.00 (H_e, dddd, J_{ec} 2.4, J_{ef} 2.6, J_{eg} 7.0, J_{ed} 14 Hz), 1.80 (H_g, ddddd, J_{gi} 1.2, J_{ge} 7.0, J_{gd} 10.4, J_{gh} 12.1, J_{gf} 14 Hz), 1.51 (3 × H_a, d, J_{ab} 6.0 Hz), 1.46 (H_d, dddd, J_{df} 7.1, J_{dg} 10.4, J_{dc} 12.0, J_{de} 14.0 Hz). We assign structure (**4a**) to this major invertomer from analysis of coupling constants and hence dihedral angles. The larger geminal coupling constants for J_{jk} and J_{hl} (17.3 and 15.2 Hz respectively) are consistent with widening of the ring bond angles at these two positions.[4]

Sufficient signals from the minor invertomer (**4b**) are visible including δ($CDCl_3$) 8.17 (H_o, dd, J_{om} 1.6, J_{on} 8.0 Hz), 7.67 (H_m, ddd, J_{mo} 1.6, J_{mn} 7.0, J_{ml} 8.2 Hz), 7.58 (H_l, dd, J_{ln} 1.1, J_{lm} 8.2 Hz), 7.37 (H_n, ddd, J_{nl} 1.1, J_{nm} 7.0, J_{no} 8.0 Hz), 3.19 (H_k, ddd, J_{kl} 1.1, J_{kh} 11.9, J_{kj} 13.2 Hz), 2.91 (H_j, ddd, J_{jh} 1.2, J_{jl} 8.4, J_{jk} 13.2 Hz), 2.60 (H_c, ddd, J_{ce} 1.2, J_{ca} 7.1, J_{cd} 10.8 Hz) to allow the all-*cis* structure (**4b**) to be assigned to it. The similarity to the eight-membered ring conformation in (**2**) results in a high field methyl doublet (δ 1.13, *J* 6.3 Hz) as a result of the shielding effect of the C=O group. Not surprisingly, the spectrum of the major invertomer (**4a**) bears little resemblance to that of (**2**).

If a crystalline sample of this aziridine from oxidation of (**3**) is dissolved in $CDCl_3$, pre-cooled to −20 °C, and its n.m.r. spectrum measured at this temperature, signals from the minor component (**4b**) are absent and only appear as the temperature is raised to +20 °C. We interpret this result as a preferential crystallisation of (**4a**) (a second-order asymmetric transformation) and the fact that the temperature at which inversion is occurring at a detectable rate is similar to that measured in other aziridines[5] suggests that the relationship between major and minor components is one of invertomers rather than conformational isomers.

Presumably it is the strain resulting from three groups *cis* on an aziridine ring in (**4b**), and the mitigation in (**4a**) of some of the usual strain factors in medium-ring compounds, which lead to a preference for the *trans*-fused ring junction in (**4a**).

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References

1 R. S. Atkinson, B. D. Judkins, and N. Khan, *J. Chem. Soc., Perkin Trans.* 1, 1982, 2491.
2 *Cf.* the conformational analysis of cyclo-octene epoxide: F. A. L. Anet and I. Yavari, *J. Am. Chem. Soc.*, 1978, **100**, 7814.
3 Intermolecular additions of *N*-nitrenes to alkenes are invariably stereospecific: R. S. Atkinson and C. W. Rees, *J. Chem. Soc. C*, 1969, 772; D. W. Jones, *J. Chem. Soc., Chem. Commun.*, 1972, 884; T. L. Gilchrist, C. W. Rees, and E. Stanton, *J. Chem. Soc. C*, 1971, 988.
4 L. M. Jackman and S. Sternhell, 'Applications of Nuclear Magnetic Resonance in Organic Chemistry,' Pergamon Press, Oxford, 1969, p. 275.
5 R. S. Atkinson and J. R. Malpass, *J. Chem. Soc., Perkin Trans.* 1, 1977, 2242.