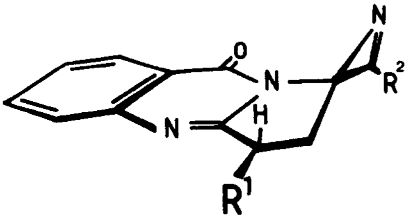
Tetrahedron Letters,Vol.26,No.36,pp 4399-4402,1985 0040-4039/85 $3.00 + .00
Printed in Great Britain

CONFORMATIONAL ANALYSIS OF SPIRO- AND RING-FUSED AZIRINES

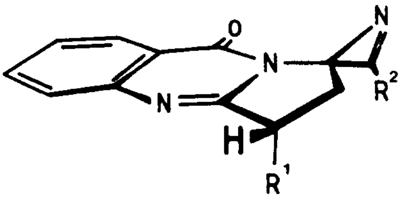
Robert S. Atkinson* and Michael J. Grimshire
Department of Chemistry, Leicester University, Leicester LE1 7RH

SUMMARY: The azirines (6) and (7) are shown to be anchored in solution in the conformations shown: it is suggested that these and the envelope conformations in (1)-(4) are stabilised by an interaction between the quinazolone nitrogen (N-3) p-orbital and a (bonded) p-orbital on the adjacent azirine carbon atom (the spiro-centre in (1)-(4) and (6)).

We recently reported that the 5-membered rings of the spiro-fused azirines (1)-(4) are apparently locked in the envelope conformation shown.[1] This conclusion was drawn from an X-ray crystal structure determination on (2) together with a comparison of the n.m.r. spectra of (1)-(4). The structure in the crystal of (2), which we presume to be that in solution also, shows a remarkable deformation of bond angles at the spiro-centre: the C-C bond of the azirine ring is only 5.9° out of plane defined by the C-N and C-C five-membered ring bonds to the spiro-centre whereas the C-N bond of the azirine ring is at an angle of 44.5° to this plane.



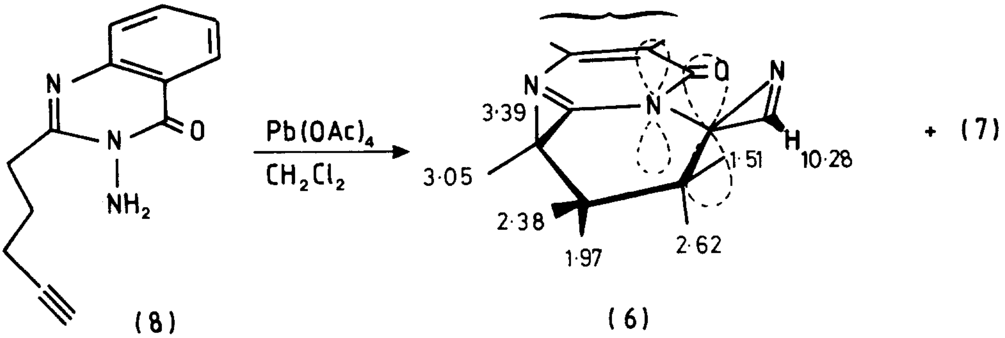
(1) $R^1 = R^2 = H$
(2) $R^1 = H$, $R^2 = Me$
(3) $R^1 = CH_2C{\equiv}CH$, $R^2 = H$
(4) $R^1 = CH_2C{\equiv}CMe$, $R^2 = Me$



(5)

This deformation at the spiro-centre in (1)-(4), however, does not obviously bring about the anchoring of the five-membered ring envelope conformation as shown in the diagram since there is an alternative conformation (5) with the 'flap' of the envelope up (above the plane defined by the quinazolone ring) which has similar bond angles at the spiro-centre to those in (1)-(4). Conceivably conformation (5) is less favourable for (3) and (4) because of the requirement for an 'axial' rather than an 'equatorial' disposition of R^1 but this cannot be the case for (1) and (2).

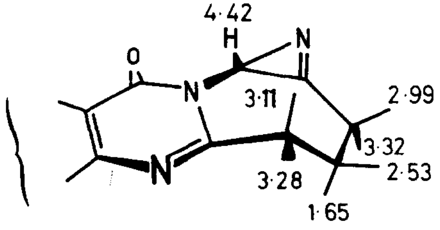
In this letter we describe the conformations of two closely related azirines (6) and (7) and suggest an explanation for the anchoring present in (1)-(4), (6) and probably (7) also. Oxidation of the N-aminoquinazolone (8) in dichloromethane gave a mixture of (6) and (7) in a ratio of 9:4, respectively. Azirine (6) was separated by crystallisation from ethanol and comparison of the n.m.r. spectrum of the crystalline material with that of the crude reaction product (which contained (6) and (7) only) showed no loss or modification of signals assignable to (6).



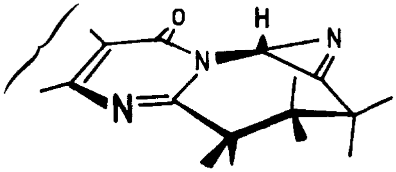
(8) (6)

The conformation of (6), which can be deduced from the vicinal coupling constants in its n.m.r. spectrum of protons in the trimethylene chain (δ3.39 J 11.9 and 5.9; 3.05 J 5.6 and 5.1; 2.62 J 8.9, 4.6 and 2.3; 2.38 J 8.9, 5.9, 5.1 and 4.6; 1.97 J 11.9, 8.9, 7.2 and 5.6; 1.51 J 8.9 and 7.2 Hz) is a twist-boat as shown. Both half-chair conformations and the alternative twist-boat can be eliminated; the former because of the absence of axial-axial coupling and the latter because of the similarity of the protons on the methylene group adjacent to the spiro-centre to those in (2) both in chemical shift (δ1.52 v. 1.75 and 2.62 v. 2.65, respectively) and coupling constant to the azirine ring H (J 2.3 v. 2.8 Hz to the lower field resonance in each case).

The ring-fused azirine (7) has not been separated from (6) but in the 400 MHz spectrum of the mixture, signals from (7) are sufficiently separated from those of (6) for its structure to be assigned. Again the vicinal coupling contants in the trimethylene unit define the conformation of the molecule as shown in (7) (δ3.32 J 5 and 1.5; 3.28 J 7.7 and 1.5; 3.11 J 12.3 and 1.5; 2.99 J 12.7 and 7.7; 2.55 J 7.7, 7.7, 1.5, and 1.5; 1.65 J 12.7, 12.3, 5 and 1.5 Hz). Examination of models suggests that there is an accessible alternative conformation (9) for this ring-fused azirine in which there is better staggering of bonds in this trimethylene chain but which, nevertheless, can be excluded from the size of the coupling contants referred to above.

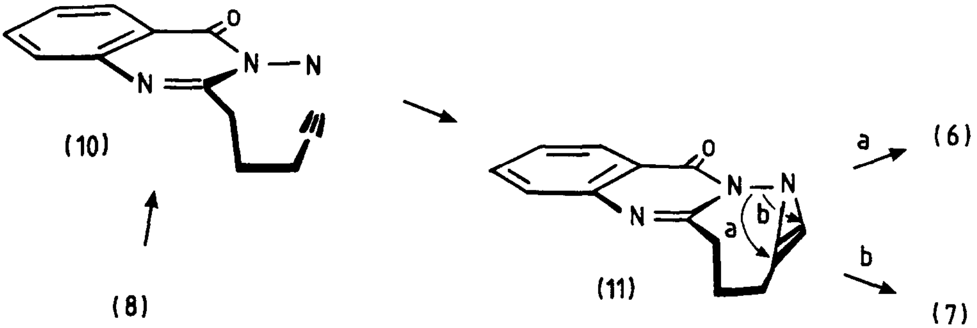


(7)



(9)

What is the origin of the conformational anchoring effect in (1)-(4) and why are the azirines derived by oxidation of (8) anchored in what appear to be their less stable conformations (6) and (7)? The near planarity at the spiro-centre in (2) referred to earlier is believed to be the result of a hybridisation at this centre which is close to sp^2 with the p-orbital utilised in C-N (azirine) bond formation. We suggest that in the preferred conformations shown for (1)-(4), (6) and probably also (7), there is an alignment of this (bonded) p-orbital with the p-orbital of the quinazolone ring nitrogen (see (6)) and the interaction which results leads to a lowering of energy and a stabilisation of these conformations over others. It is clear from examination of (1)-(4) and (6) that the slight tilting of the p-orbital at the spiro-centre which is anticipated (the three bonds at this centre referred to earlier are not completely planar) would serve to increase this alignment in the preferred conformations of the azirines shown but to decrease it in other possible conformations.



Scheme

Oxidation of N-aminoquinazolone (8) generates the corresponding N-nitrene (10) which adds to the acetylenic bond and (6) and (7) are believed to be formed by rearrangement of the unstable 1H-azirine intermediate (11) (Scheme).[2] By analogy with the corresponding intramolecular addition of N-nitrenes to alkenes,[3] nitrene addition to the alkyne bond would be expected to take place as shown and would lead to the conformation of 1H-azirine indicated. It is noteworthy that migration of the N-N bond in the two modes a and b as shown delivers (6) and (7) directly in their most stable conformations. We do not think this augurs well for the prospect of trapping the 1H-azirines in this system.

Since the near-planarity at the spiro-centre in (2) is also present at C-3 in all other published crystal structures of azirines[1] and is therefore, presumably, common to all azirines, further conformational manifestations of this effect can be anticipated in spiro- or ring-fused azirines.

We thank the University of Warwick 400 MHz n.m.r. service (S.E.R.C.) for spectra and S.E.R.C. for support to M.J.G.

References

1. R.S. Atkinson, J. Fawcett, M.J. Grimshire, and D.R. Russell, *J. Chem. Soc., Chem. Commun.*, 1985, 544.
2. D.J. Anderson, T.L. Gilchrist, G.E. Gymer, and C.W. Rees, *J. Chem. Soc., Perkin Trans. I*, 1973, 550.
3. R.S. Atkinson, J.R. Malpass, K.L. Skinner, and K.L. Woodthorpe, *J. Chem. Soc., Perkin Trans. I*, 1984, 1905.

(Received in UK 8 July 1985)